

IMPACT OF SPATIALLY HETEROGENEOUS TEMPERATURE ON THE DYNAMICS OF DENGUE EPIDEMICS

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ABSTRACT. In recent years, the growing spatial spread of dengue, a mosquito-borne disease, has been a major international public health concern. In this paper, we propose a mathematical model to describe an impact of spatially heterogeneous temperature on the dynamics of dengue epidemics. We first consider homogeneous temperature profiles across space and study sensitivity of the basic reproduction number to the environmental temperature. We then introduce spatially heterogeneous temperature into the model and establish some important properties of dengue dynamics. In particular, we formulate two indices, mosquito reproduction number and infection invasion threshold, which completely determine the global threshold dynamics of the model. We also perform numerical simulations to explore the impact of spatially heterogeneous temperature on the disease dynamics. Our analytical and numerical results reveal that spatial heterogeneity of temperature can have significant impact on expansion of dengue epidemics. Our results, including threshold indices, may provide useful information for effective deployment of spatially targeted interventions.

1. Introduction. Dengue, a mosquito-borne viral disease, has become one of the major public health concerns as 2.5 billions people are currently living in areas of risk of dengue, and about 390 million new dengue infections occur annually worldwide [2, 41]. In comparison to only nine countries affected by dengue epidemics in the 1970's, current reports of dengue outbreaks in more than a hundred countries show that dengue fever is one of the most rapidly spreading mosquito-borne viral diseases in the world [2, 35, 41]. Because of this remarkably growing spatial spread of dengue, studies on dengue epidemics across space are becoming increasingly important.

While causes for increase in dengue cases may include a combination of multiple factors such as range expansion of its primary vector (the mosquito *Aedes aegypti*), inefficient vector control, human population growth and urbanization [1, 10, 24,

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29, 34], the majority of them are thought to link to human and vector mobility and climatic factors [1, 2, 24, 26]. In particular, the environmental temperature has been found to highly affect the transmission dynamics of dengue [2, 25, 35]. Also, continuous increase of global temperature has predicted that the endemic range of dengue will keep expanding geographically [1, 9, 11, 15, 25, 42]. Therefore, it is critical to understand the role of temperature heterogeneity on geographical expansion of dengue epidemics.

Experimental studies show that the environmental temperature can highly and nonlinearly affect many mosquito entomological parameters [44, 45], such as oviposition rate, mortality rate and maturation rate, as well as some dengue dynamics parameters, such as incubation period and transmission rates [7, 17]. Combined studies of such nonlinear effects of spatially heterogeneous temperature and mobility of human and vector can advance our understanding of dengue transmission dynamics. Since there is no vaccine for dengue [2, 30] and the current dengue control relies on limiting mosquito population [2, 30, 44], inclusion of detailed effects of environmental temperature on mosquito entomology into the models of dengue spread may provide useful information for proper implementation of prevention and control measures.

Previous quantitative studies on dengue epidemics have provided significant understanding of temporal dynamics [17, 18, 27, 23, 43] and spatial spread [6, 15, 24, 25, 35] of dengue. However, none of the existing models have considered nonlinear heterogeneous temperature that might have significant impact on disease outcomes and prevention effectiveness. In this study, we propose a transmission dynamics model of dengue that incorporates both mobility of human and vector as well as nonlinear effects of spatial heterogeneity on the environmental temperature. We introduce into the model a spatial diffusion of human and vector population and use experimentally-determined dependence of entomological and dengue dynamics parameters on the environmental temperature. We focus on how spatial diffusion and spatial temperature heterogeneity affect the infection invasion threshold and the dynamics of dengue epidemics.

The rest of the paper is organized as follows. The model is formulated in Section 2. The model analysis and simulation results are presented in Sections 3 and 4, respectively. Finally, we state some conclusions of the paper in Section 5.

2. Model. Suppose $\Omega \subset \mathbb{R}^n$ is a bounded domain which contains human and female mosquito populations. We divide the total human population into susceptible (H_s), exposed (H_e), infected (H_i) and recovered (H_r) groups. We also divide the total female mosquito population into aquatic (A), susceptible (M_s), exposed (M_e), and infected (M_i) groups. We introduce the human and mosquito mobility by spatial diffusion terms in the model. Following experimental evidences [7, 17, 44], we incorporate the effects of environmental temperature via entomological and dengue dynamics parameters.

The model we consider is as follows:

$$\frac{\partial A}{\partial t} = k\delta(x) \left(1 - \frac{A}{C}\right) (M_s + M_e + M_i) - (\theta(x) + \mu_a(x))A, \quad (2.1)$$

$$\frac{\partial M_s}{\partial t} = D_M \Delta M_s + \theta(x)A - \frac{b\beta_m(x)M_s H_i}{H_s + H_e + H_i + H_r} - \mu_m(x)M_s, \quad (2.2)$$

$$\frac{\partial M_e}{\partial t} = D_M \Delta M_e + \frac{b\beta_m(x)M_s H_i}{H_s + H_e + H_i + H_r} - (\gamma_m(x) + \mu_m(x))M_e, \quad (2.3)$$

$$\frac{\partial M_i}{\partial t} = D_M \Delta M_i + \gamma_m(x)M_e - \mu_m(x)M_i, \quad (2.4)$$

$$\frac{\partial H_s}{\partial t} = D_H \Delta H_s + \Lambda_h(x) - \mu_h H_s - \frac{b\beta_h(x)H_s M_i}{H_s + H_e + H_i + H_r}, \quad (2.5)$$

$$\frac{\partial H_e}{\partial t} = D_H \Delta H_e + \frac{b\beta_h(x)H_s M_i}{H_s + H_e + H_i + H_r} - (\gamma_h + \mu_h)H_e, \quad (2.6)$$

$$\frac{\partial H_i}{\partial t} = D_H \Delta H_i + \gamma_h H_e - (\alpha_h + \mu_h)H_i, \quad (2.7)$$

$$\frac{\partial H_r}{\partial t} = D_H \Delta H_r + \alpha_h H_i - \mu_h H_r. \quad (2.8)$$

with $(x, t) \in \Omega \times (0, \infty)$. Here, $\Lambda_h(x)$ represents the birth or recruitment rate of susceptible human population. D_M and D_H are the diffusion coefficients related to mosquito and human, respectively, and Δ is the Laplace operator. In the model, the aquatic mosquito population, A , represents both larvae and pupae. Matured mosquitos ($M_s + M_e + M_i$) produce aquatic mosquitos with a per capita oviposition rate $\delta(x)(1 - \frac{A}{C})$, where $\delta(x)$ is the intrinsic oviposition rate and C is the carrying capacity of the mosquito aquatic phase. Parameter k represents a combination of the fraction of eggs hatching to larvae and the fraction of female mosquitoes hatched from all eggs. As a result, the net increase of aquatic mosquito population is $k\delta(x)(1 - \frac{A}{C})(M_s + M_e + M_i)$ per unit time. Female mosquitoes emerge from the aquatic phase with a rate $\theta(x)$ and we assume that these newly emerged female mosquitos are all susceptible. Parameters $\mu_a(x)$, $\mu_m(x)$, and μ_h represent natural mortality rate of aquatic population, mosquito population, and human population, respectively.

Susceptible mosquitoes get infected when they bite infected humans with a per capita transmission rate $b\beta_m(x)H_i/(H_s + H_e + H_i + H_r)$, where b is the per capita biting rate of mosquitoes and $\beta_m(x)$ represents the transmission probability from human to mosquito. We acknowledge that biting rates may also depend on the environmental temperature. Because of lack of explicit data on the functional relationship between the environmental temperature and biting rates, we take b to be constant in this study. However, as the net transmission rate $b\beta_m(x)$ is a function of x , all theorems developed in this paper are also applicable to cases in which b depends on x . Exposed mosquitos become infectious at a rate $\gamma_m(x)$ equivalent to an average extrinsic period $1/\gamma_m(x)$. Similarly, susceptible humans get infected by mosquito bites with a per capita transmission rate $b\beta_h(x)M_i/(H_s + H_e + H_i + H_r)$, where $\beta_h(x)$ represents the transmission probability from mosquito to human. γ_h represents the rate at which exposed humans become infectious, corresponding to intrinsic period $1/\gamma_h$, and infected humans get recovered from dengue at a rate α_h . As mentioned in Bhatt et al. [2], we assume that these recovered humans do not loose immunity during the period of dynamics considered. Since dengue virus is generally non-pathogenic [2, 30], we ignore disease caused deaths in our model.

Here, we use the following homogeneous Neumann boundary conditions

$$\begin{aligned} \frac{\partial M_s(x,t)}{\partial \nu} &= \frac{\partial M_e(x,t)}{\partial \nu} = \frac{\partial M_i(x,t)}{\partial \nu} = 0 \\ \frac{\partial H_s(x,t)}{\partial \nu} &= \frac{\partial H_e(x,t)}{\partial \nu} = \frac{\partial H_i(x,t)}{\partial \nu} = \frac{\partial H_r(x,t)}{\partial \nu} = 0, \end{aligned} \quad (2.9)$$

$$x \in \partial\Omega, t > 0,$$

and the following initial conditions

$$\begin{aligned} A(x, 0) &= A^0(x), \quad M_s(x, 0) = M_s^0(x), \quad M_e(x, 0) = M_e^0(x), \quad M_i(x, 0) = M_i^0(x), \\ H_s(x, 0) &= H_s^0(x), \quad H_e(x, 0) = H_e^0(x), \quad H_i(x, 0) = H_i^0(x), \quad H_r(x, 0) = H_r^0(x), \\ x &\in \Omega, \end{aligned} \tag{2.10}$$

where $\frac{\partial}{\partial\nu}$ denotes the differentiation along the outward normal ν to $\partial\Omega$. We note that in the absence of diffusions and spatially homogeneous environment, our system (2.1)-(2.10) recovers the ODE system of dengue model proposed previously in [27].

2.1. Entomological parameters. We consider the environmental temperature profile, $T(x)$, that captures a heterogeneity of temperature across the domain Ω . We obtained the data from an experimental study [44, 45], in which the dependence of oviposition rate, aquatic phase mortality rate, rate of emergence of female mosquito from aquatic phase, and female mosquito mortality rate on temperature were studied. Based on the patterns observed in the data, we fitted the data to appropriate functional curves (Fig. 2.1). Our data fitting exercise provides the following relationships:

$$\delta(x) = \frac{\delta_m T(x)^{N_\delta}}{\delta_h^{N_\delta} + T(x)^{N_\delta}}, \tag{2.11}$$

$$\mu_a(x) = a_{0\mu_a} + a_{1\mu_a} T(x) + a_{2\mu_a} T(x)^2 + a_{3\mu_a} T(x)^3 + a_{4\mu_a} T(x)^4, \tag{2.12}$$

$$\theta(x) = \begin{cases} 0, & T(x) < a_{1\theta}, \\ a_{0\theta} T(x) (T(x) - a_{1\theta}) \sqrt{a_{2\theta} - T(x)}, & a_{1\theta} \leq T(x) \leq a_{2\theta}, \\ 0, & T(x) > a_{2\theta}. \end{cases} \tag{2.13}$$

$$\mu_m(x) = a_{0\mu_m} + a_{1\mu_m} T(x) + a_{2\mu_m} T(x)^2. \tag{2.14}$$

2.2. Dengue dynamics parameters. The incubation time period of dengue, i.e. the average duration for which mosquitos stay in exposed class before they become infectious, depends on temperature. In this study, we followed a previously developed function derived based on an enzyme kinetic model [7, 17], which provides

$$\gamma_m(x) = \frac{1}{a_{0\gamma_m}} e^{a_{1\gamma_m} T(x)}. \tag{2.15}$$

Accurate data of the transmission probability from humans to mosquitos and that from mosquitos to humans are not available. However, using rich empirical data related to many other mosquito-flavivirus (West Nile virus, Murray Valley encephalitis virus, and St. Louis encephalitis virus), Lambrechts et al. [17] have provided reasonable estimates of Dengue transmission probability. As estimated previously [17], the transmission probability from humans to mosquitos remains negligible up to certain minimum temperature and increases linearly until it reaches one at a maximum temperature and remains one for temperatures higher than the maximum temperature. This trend can be described using E-max model (Fig. 2.2) given by the following expression:

$$\beta_m(x) = \frac{T(x)^{N_{\beta_m}}}{\beta_{mh}^{N_{\beta_m}} + T(x)^{N_{\beta_m}}}. \tag{2.16}$$

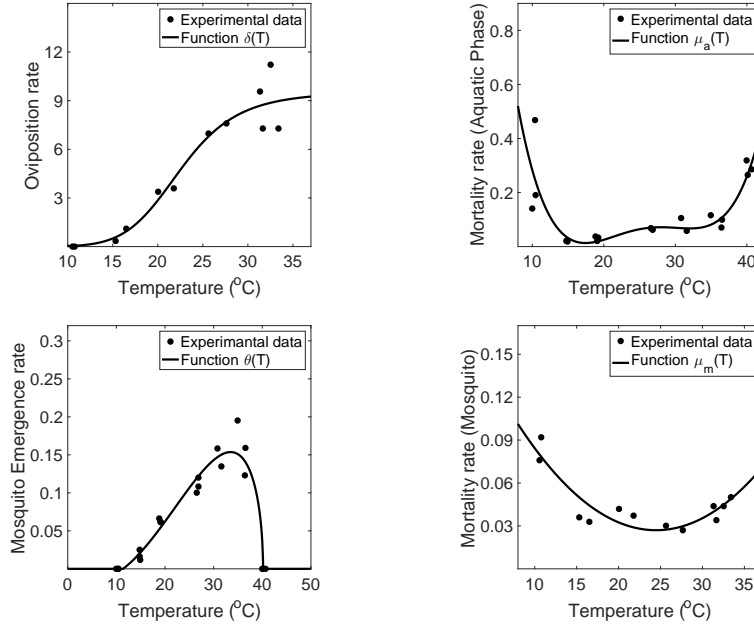


FIGURE 2.1. Functional curves $\delta(T)$, oviposition rate, $\mu_a(T)$, aquatic phase mortality rate, $\theta(T)$, mosquito emergence rate from acuatic phase, and $\mu_m(T)$, mosquito mortality rate, fitted to the experimental data [44]

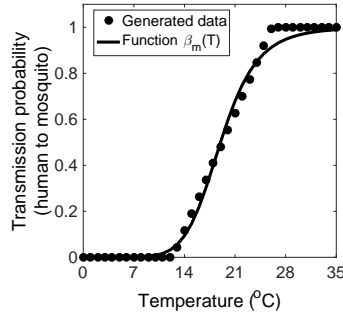


FIGURE 2.2. Functional curve $\beta_m(T)$, the transmission probability from human to mosquito, fitted to the data generated from the previous estimates [17]

For a temperature dependence of the transmission probability from mosquitoes to humans, we approximate it to the proportion of midgut-infected mosquitoes transmitting virus as done in Lambrechts et al. [17]. Accordingly, a functional relationship between the transmission probability from mosquitoes to humans and temperature is given by

$$\beta_h(x) = \begin{cases} 0, & T(x) < a_{1\beta_h}, \\ a_{0\beta_h} T(x) (T(x) - a_{1\beta_h}) \sqrt{a_{2\beta_h} - T(x)}, & a_{1\beta_h} \leq T(x) \leq a_{2\beta_h}, \\ 0, & T(x) > a_{2\beta_h}. \end{cases} \quad (2.17)$$

TABLE 2.1. Model parameters

Parameter	Description	Value	Reference
k	fraction of female larvae from eggs	0.5 (0-1)	[18, 27]
b	per capita biting rate	0.1	[4, 27]
μ_h	Natural death rate of humans	$4.22 \times 10^{-5} \text{ d}^{-1}$	Calculated, [16]
$1/\gamma_h$	Intrinsic period	10 days	[4, 16, 18, 27]
α_h	Human recovery rate	0.1 d^{-1}	[18, 27]
D_M, D_H	Diffusion coefficients	-	varied
δ_m	In $\delta(x)$	9.531	Data fitting
δ_h	In $\delta(x)$	22.55	Data fitting
N_δ	In $\delta(x)$	7.084	Data fitting
$a_{0\mu_a}$	In $\mu_a(x)$	2.914	Data fitting
$a_{1\mu_a}$	In $\mu_a(x)$	-0.4986	Data fitting
$a_{2\mu_a}$	In $\mu_a(x)$	0.03099	Data fitting
$a_{3\mu_a}$	In $\mu_a(x)$	-0.0008236	Data fitting
$a_{4\mu_a}$	In $\mu_a(x)$	7.975×10^{-6}	Data fitting
$a_{0\theta}$	In $\theta(x)$	8.044×10^{-5}	Data fitting
$a_{1\theta}$	In $\theta(x)$	11.386	Data fitting
$a_{2\theta}$	In $\theta(x)$	40.1461	Data fitting
$a_{0\mu_m}$	In $\mu_m(x)$	0.1901	Data fitting
$a_{1\mu_m}$	In $\mu_m(x)$	-0.0134	Data fitting
$a_{2\mu_m}$	In $\mu_m(x)$	2.739×10^{-4}	Data fitting
$a_{0\gamma_m}$	In $\gamma_m(x)$	$5 \times 10^{4/3}$	Data fitting
$a_{1\gamma_m}$	In $\gamma_m(x)$	0.0768	Data fitting
β_{mh}	In $\beta_m(x)$	18.9871	Data fitting
N_{β_m}	In $\beta_m(x)$	7	Data fitting
$a_{0\beta_h}$	In $\beta_h(x)$	1.044×10^{-3}	Data fitting
$a_{1\beta_h}$	In $\beta_h(x)$	12.286	Data fitting
$a_{2\beta_h}$	In $\beta_h(x)$	32.461	Data fitting

The model parameters are given in Table 2.1.

3. **Model analysis.** For convenience, we assume that

$$(u_1, u_2, u_3, u_4, u_5, u_6, u_7, u_8) = (A, M_s, M_e, M_i, H_s, H_e, H_i, H_r).$$

Then system (2.1)-(2.10) becomes

$$\begin{cases} \frac{\partial u_1}{\partial t} = k\delta(x) \left(1 - \frac{u_1}{C}\right) (u_2 + u_3 + u_4) - (\theta(x) + \mu_a(x))u_1, & x \in \Omega, t > 0, \\ \frac{\partial u_2}{\partial t} = D_M \Delta u_2 + \theta(x)u_1 - \frac{b\beta_m(x)u_2u_7}{u_5+u_6+u_7+u_8} - \mu_m(x)u_2, & x \in \Omega, t > 0, \\ \frac{\partial u_3}{\partial t} = D_M \Delta u_3 + \frac{b\beta_m(x)u_2u_7}{u_5+u_6+u_7+u_8} - (\gamma_m(x) + \mu_m(x))u_3, & x \in \Omega, t > 0, \\ \frac{\partial u_4}{\partial t} = D_M \Delta u_4 + \gamma_m(x)u_3 - \mu_m(x)u_4, & x \in \Omega, t > 0, \\ \frac{\partial u_5}{\partial t} = D_H \Delta u_5 + \Lambda_h(x) - \mu_h u_5 - \frac{b\beta_h(x)u_5u_4}{u_5+u_6+u_7+u_8}, & x \in \Omega, t > 0, \\ \frac{\partial u_6}{\partial t} = D_H \Delta u_6 + \frac{b\beta_h(x)u_5u_4}{u_5+u_6+u_7+u_8} - (\gamma_h + \mu_h)u_6, & x \in \Omega, t > 0, \\ \frac{\partial u_7}{\partial t} = D_H \Delta u_7 + \gamma_h u_6 - (\alpha_h + \mu_h)u_7, & x \in \Omega, t > 0, \\ \frac{\partial u_8}{\partial t} = D_H \Delta u_8 + \alpha_h u_7 - \mu_h u_8, & x \in \Omega, t > 0, \\ \frac{\partial u_i}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, 2 \leq i \leq 8, \\ u_i(x, 0) = u_i^0(x), & x \in \Omega, t > 0, 1 \leq i \leq 8. \end{cases} \quad (3.1)$$

Let $\mathbb{X} := C(\bar{\Omega}, \mathbb{R}^8)$ be the Banach space with the supremum norm $\|\cdot\|_{\mathbb{X}}$. Define $\mathbb{X}^+ := C(\bar{\Omega}, \mathbb{R}_+^8)$, then $(\mathbb{X}, \mathbb{X}^+)$ is a strongly ordered space. Let $\phi = (\phi_1, \phi_2, \phi_3, \phi_4, \phi_5, \phi_6, \phi_7, \phi_8)$ and

$$\mathbb{X}_C := \{\phi \in \mathbb{X}^+ : 0 \leq \phi_1(x) \leq C, \forall x \in \bar{\Omega}\}. \quad (3.2)$$

By the similar arguments in [14, Lemma 2.2] (see also [19]), together with [21, Corollary 4] (see also [31, Theorem 7.3.1]), we have the following result:

Lemma 3.1. *For every initial value function $\phi \in \mathbb{X}_C$, system (3.1) has a unique mild solution $u(x, t, \phi)$ on $(0, \tau_\phi)$ with $u(\cdot, 0, \phi) = \phi$, where $\tau_\phi \leq \infty$. Furthermore, $u(\cdot, t, \phi) \in \mathbb{X}_C, \forall t \in (0, \tau_\phi)$ and $u(x, t, \phi)$ is a classical solution of (3.1).*

Note that for the following scalar reaction-diffusion equation

$$\begin{cases} \frac{\partial w}{\partial t} = D\Delta w + g(x) - d(x)w, & x \in \Omega, t > 0, \\ \frac{\partial w}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, \end{cases} \quad (3.3)$$

where $D > 0$, and $d(x)$ and $g(x)$ are continuous and positive functions on $\bar{\Omega}$, we have the following result.

Lemma 3.2. [19, Lemma 1] *The system (3.3) admits a unique positive steady state $w^*(x)$ which is globally asymptotically stable in $C(\bar{\Omega}, \mathbb{R}_+)$. Moreover, if $g(x) \equiv g, d(x) \equiv d, \forall x \in \bar{\Omega}$, then $w^*(x) = \frac{g}{d}$.*

In the next Lemma, we now show that solutions of system (3.1) exist globally on $[0, \infty)$ and converge to a compact attractor in \mathbb{X}_C .

Lemma 3.3. *For every initial value functions $\phi \in \mathbb{X}_C$, system (3.1) admits a unique solution $u(x, t, \phi)$ on $[0, \infty)$ with $u(\cdot, 0, \phi) = \phi$ and the semiflow $\Psi(t) : \mathbb{X}_C \rightarrow \mathbb{X}_C$ generated by (3.1) is defined by*

$$\Psi(t)\phi = u(\cdot, t, \phi), \quad t \geq 0.$$

Furthermore, the semiflow $\Psi(t) : \mathbb{X}_C \rightarrow \mathbb{X}_C$ has a global compact attractor in $\mathbb{X}_C, \forall t \geq 0$.

Proof. Let

$$N_H(x, t) = u_5(x, t) + u_6(x, t) + u_7(x, t) + u_8(x, t). \quad (3.4)$$

From (3.1), we have that $N_H(x, t)$ satisfies

$$\begin{cases} \frac{\partial N_H}{\partial t} = D_H \Delta N_H + \Lambda_h(x) - \mu_h N_H, & x \in \Omega, t > 0, \\ \frac{\partial N_H}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (3.5)$$

By Lemma 3.2, the system (3.5) admits a positive function $H(x)$ such that

$$\lim_{t \rightarrow \infty} N_H(x, t) = H(x), \quad \text{uniformly in } x \in \bar{\Omega}. \quad (3.6)$$

Furthermore, if $\Lambda_h(x) \equiv \Lambda_h$, a constant, then $H(x) \equiv \frac{\Lambda_h}{\mu_h}$.

Let

$$M(x, t) = u_2(x, t) + u_3(x, t) + u_4(x, t). \quad (3.7)$$

Then it follows from the first four equations of (3.1) that $(u_1(x, t), M(x, t))$ satisfies

$$\begin{cases} \frac{\partial u_1}{\partial t} = k\delta(x) \left(1 - \frac{u_1}{C}\right) M - (\theta(x) + \mu_a(x))u_1, & x \in \Omega, t > 0, \\ \frac{\partial M}{\partial t} = D_M \Delta M + \theta(x)u_1 - \mu_m(x)M, & x \in \Omega, t > 0, \\ \frac{\partial M}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (3.8)$$

Lemma 3.1 along with (3.4), (3.5), (3.6), and the comparison principle imply that $u_5(x, t, \phi)$, $u_6(x, t, \phi)$, $u_7(x, t, \phi)$, and $u_8(x, t, \phi)$ are uniformly bounded and ultimately bounded. Similarly, Lemma 3.1 along with (3.7), (3.8), and the comparison principle imply that $u_1(x, t, \phi)$, $u_2(x, t, \phi)$, $u_3(x, t, \phi)$, and $u_4(x, t, \phi)$ are uniformly bounded. Next, we show that $u_i(x, t, \phi)$, $i = 1, 2, 3, 4$, is ultimately bounded. By Lemma 3.1, we have

$$u_1(x, t, \phi) \leq C, \text{ for } x \in \bar{\Omega}, t \geq 0. \quad (3.9)$$

It then follows from the second equation of (3.1) that

$$\begin{cases} \frac{\partial u_2}{\partial t} \leq D_M \Delta u_2 + C\theta(x) - \mu_m(x)u_2, & x \in \Omega, t > 0, \\ \frac{\partial u_2}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (3.10)$$

By (3.10), Lemma 3.2, and a comparison argument, it is easy to see that $u_2(x, t, \phi)$ is ultimately bounded. Using (3.6), together with the facts that $u_2(x, t, \phi)$ and $u_7(x, t, \phi)$ are ultimately bounded, there exists $T_1 > 0$ and $C_1 > 0$ such that

$$N_H(x, t) \geq H(x)/2, \quad u_2(x, t, \phi)u_7(x, t, \phi) \leq C_1, \text{ for } x \in \bar{\Omega}, t \geq T_1. \quad (3.11)$$

From (3.11) and the third equation of (3.1), we have

$$\begin{cases} \frac{\partial u_3}{\partial t} \leq D_M \Delta u_3 + \frac{b\beta_m(x)C_1}{H(x)/2} - (\gamma_m(x) + \mu_m(x))u_3, & x \in \Omega, t \geq T_1, \\ \frac{\partial u_3}{\partial \nu} = 0, & x \in \partial\Omega, t \geq T_1. \end{cases} \quad (3.12)$$

By (3.12), Lemma 3.2, and a comparison argument, it is easy to see that $u_3(x, t, \phi)$ is ultimately bounded, and hence, there exists $T_2 > 0$ and $C_2 > 0$ such that

$$u_3(x, t, \phi) \leq C_2, \text{ for } x \in \bar{\Omega}, t \geq T_2. \quad (3.13)$$

From (3.13) and the fourth equation of (3.1), we have

$$\begin{cases} \frac{\partial u_4}{\partial t} \leq D_M \Delta u_4 + \gamma_m(x)C_2 - \mu_m(x)u_4, & x \in \Omega, t \geq T_2, \\ \frac{\partial u_4}{\partial \nu} = 0, & x \in \partial\Omega, t \geq T_2. \end{cases} \quad (3.14)$$

Again, using (3.12), Lemma 3.2, and a comparison argument, we deduce that $u_4(x, t, \phi)$ is ultimately bounded. Thus, $\Psi(t)$ is point dissipative on \mathbb{X}_C (ultimately bounded), and forward orbits of bounded subsets of \mathbb{X}_C for $\Psi(t)$ are bounded (uniformly bounded). We note that the first equation in (3.1) has no diffusion term, so its solution semiflow $\Psi(t)$ is not compact. Since $-(\theta(x) + \mu_a(x)) < 0$, $\forall x \in \bar{\Omega}$, we can use similar arguments as in [13, Theorem 4.1] (see also [12, Lemma 4.1] and [20, Theorem 2.6]), and show that $\Psi(t)$ admits a global attractor on \mathbb{X}_C . \square

3.1. Homogeneous environment: Basic reproduction number. In this subsection, we consider a special case in which the temperature remains approximately constant across space, i.e. $T(x) = T$, and thus, all of $\Lambda_h(x) = \Lambda_h$, $\delta(x) = \delta$, $\theta(x) = \theta$, $\mu_a(x) = \mu_a$, $\beta_m(x) = \beta_m$, $\mu_m(x) = \mu_m$, $\gamma_m(x) = \gamma_m$, $\beta_h(x) = \beta_h$ are independent of $x \in \bar{\Omega}$.

In this case, we compute the basic reproduction number, $\bar{\mathcal{R}}_0$ which is defined as the average number of secondary infections generated by a single infected individual introduced into a completely susceptible population. We will then observe how $\bar{\mathcal{R}}_0$ depends on the environmental temperature, T .

In this case, there are two possible disease-free equilibria (DFEs): one is $\bar{E}_0 = (0, 0, 0, 0, \bar{H}^*, 0, 0, 0)$ and the other is $\bar{E}_1 = (\bar{A}^*, \bar{M}_s^*, 0, 0, \bar{H}^*, 0, 0, 0)$, where $\bar{A}^* =$

$C \left[1 - \frac{\mu_m(\theta + \mu_a)}{k\delta\theta} \right]$, $\bar{M}_s^* = \theta \bar{A}^* / \mu_m$, and $\bar{H}^* = \Lambda_h / \mu_h$. As mentioned in Remark 3.1, it can be shown that \bar{E}_0 is globally asymptotically stable and \bar{E}_1 does not exist if $\bar{\mathcal{R}}^M < 1$, where $\bar{\mathcal{R}}^M = \frac{k\delta\theta}{\mu_m(\theta + \mu_a)}$. While this situation asserts a successful avoidance of disease, it is hard to achieve practically as the situation corresponds to a complete eradication of mosquito population. Therefore, more achievable disease free situation is the asymptotic stability of \bar{E}_1 . We assume $\bar{\mathcal{R}}^M > 1$ in which \bar{E}_1 exists. We linearize the model system at \bar{E}_1 and define

$$\bar{\mathbb{F}} = \begin{pmatrix} 0 & 0 & 0 & \frac{b\beta_m \bar{M}_s^*}{\bar{H}^*} \\ 0 & 0 & 0 & 0 \\ 0 & b\beta_h & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$\bar{\mathbb{V}} = \begin{pmatrix} \gamma_m + \mu_m & 0 & 0 & 0 \\ -\gamma_m & \mu_m & 0 & 0 \\ 0 & 0 & \gamma_h + \mu_h & 0 \\ 0 & 0 & -\gamma_h & \alpha_h + \mu_h \end{pmatrix}.$$

Since $\bar{\mathbb{F}}$ and $\bar{\mathbb{V}}$ are independent of $x \in \bar{\Omega}$, it follows from [40, Theorem 3.4] that $\bar{\mathcal{R}}_0 = r(\bar{\mathbb{F}}\bar{\mathbb{V}}^{-1})$, the spectral radius of $\bar{\mathbb{F}}\bar{\mathbb{V}}^{-1}$. By direct computations, we have

$$\bar{\mathbb{V}}^{-1} = \begin{pmatrix} 1/(\gamma_m + \mu_m) & 0 & 0 & 0 \\ \gamma_m/\mu_m(\gamma_m + \mu_m) & 1/\mu_m & 0 & 0 \\ 0 & 0 & 1/(\gamma_h + \mu_h) & 0 \\ 0 & 0 & \gamma_h/(\gamma_h + \mu_h)(\alpha_h + \mu_h) & 1/(\alpha_h + \mu_h) \end{pmatrix},$$

and

$$\bar{\mathbb{F}}\bar{\mathbb{V}}^{-1} = \begin{pmatrix} 0 & 0 & D\gamma_h/(\gamma_h + \mu_h)(\alpha_h + \mu_h) & D/(\alpha_h + \mu_h) \\ 0 & 0 & 0 & 0 \\ E\gamma_m/\mu_m(\gamma_m + \mu_m) & E/\mu_m & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

where $D = \frac{b\beta_m \bar{M}_s^*}{\bar{H}^*}$ and $E = b\beta_h$. Then the characteristic polynomial of $\bar{\mathbb{F}}\bar{\mathbb{V}}^{-1}$ takes the form

$$\det(\bar{\mathbb{F}}\bar{\mathbb{V}}^{-1} - \eta I) = \eta^2(\eta^2 - \diamond),$$

where $\diamond = \frac{DE\gamma_m\gamma_h}{\mu_m(\gamma_m + \mu_m)(\gamma_h + \mu_h)(\alpha_h + \mu_h)}$. By [40, Theorem 3.4], we obtain the basic reproduction number as $\bar{\mathcal{R}}_0 = \sqrt{\diamond}$, which provides a threshold for the disease to persist ($\bar{\mathcal{R}}_0 > 1$).

In Fig. 3.1, we show how $\bar{\mathcal{R}}_0$ depends on temperature. The value of $\bar{\mathcal{R}}_0$ obtained here is consistent with the previous estimates [4, 3, 16, 33]. In addition, our study provides the dependence of $\bar{\mathcal{R}}_0$ on temperature. In general, $\bar{\mathcal{R}}_0$ is less than one for too high or too low temperatures while it is greater than one in the middle temperature range. This shows that there is an optimal temperature range for which dengue epidemics occur. Moreover, the range of optimal temperature depends upon the carrying capacity of mosquito aquatic phase. The lower the carrying capacity, the smaller the range of temperature for which $\bar{\mathcal{R}}_0 > 1$ and the lower the peak value of $\bar{\mathcal{R}}_0$. With a prevention program such as destroying mosquito larvae or pupae that significantly lowers the carrying capacity (for example, $C < 0.1$ in our

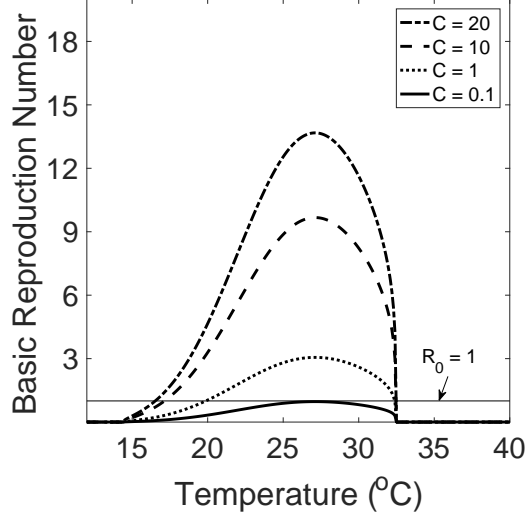


FIGURE 3.1. The basic reproduction number, $\bar{\mathcal{R}}_0$, vs. environmental temperature, T , for different values of carrying capacity, C .

computation), $\bar{\mathcal{R}}_0$ can be brought down to below one for all temperature values and dengue epidemics can be avoided (Fig. 3.1).

3.2. Heterogeneous environment. We now consider the full model that includes spatially heterogeneous temperature. The system (3.1) admits two possible DFEs: $E_0(x) = (0, 0, 0, 0, H(x), 0, 0, 0)$ and $E_1(x) = (A^*(x), M_s^*(x), 0, 0, H(x), 0, 0, 0)$. $E_0(x)$ corresponds to an eradication of mosquito population while $E_1(x)$ corresponds to an eradication of dengue in the presence of mosquito population. Practical preventive strategies, such as destroying mosquito larvae, using insecticides, and using mosquito nets, have targets of achieving one or both DFEs. Here, we develop theoretical formulation of two threshold indices: Mosquito reproduction number and Infection invasion threshold, related to the stability of $E_0(x)$ and $E_1(x)$, respectively.

3.2.1. Mosquito reproduction number. Linearizing system (3.8) at $(0, 0)$, we get

$$\begin{cases} \frac{\partial u_1}{\partial t} = k\delta(x)M - (\theta(x) + \mu_a(x))u_1, & x \in \Omega, t > 0, \\ \frac{\partial M}{\partial t} = D_M\Delta M + \theta(x)u_1 - \mu_m(x)M, & x \in \Omega, t > 0, \\ \frac{\partial M}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (3.15)$$

Let $\Pi(t)$ be the solution semigroup generated by (3.15) on $C(\bar{\Omega}, \mathbb{R}^2)$. It is easy to see that $\Pi(t)$ is a positive C_0 -semigroup on $C(\bar{\Omega}, \mathbb{R}^2)$, and its generator \mathbf{B} can be written as

$$\mathbf{B} = \begin{pmatrix} -(\theta(x) + \mu_a(x)) & k\delta(x) \\ \theta(x) & D_M\Delta - \mu_m(x) \end{pmatrix}.$$

Further, \mathbf{B} is a closed and resolvent positive operator (see, e.g., [37, Theorem 3.12]). The eigenvalue problem associated with (3.15) takes the form

$$\begin{cases} \lambda\psi_1(x) = k\delta(x)\psi_2(x) - (\theta(x) + \mu_a(x))\psi_1(x), & x \in \Omega, \\ \lambda\psi_2(x) = D_M\Delta\psi_2(x) + \theta(x)\psi_1(x) - \mu_m(x)\psi_2(x), & x \in \Omega, \\ \frac{\partial\psi_2(x)}{\partial\nu} = 0, & x \in \partial\Omega. \end{cases} \quad (3.16)$$

The first equation of (3.15) has no diffusion term, and hence, the associated solution semiflow $\Pi(t)$ is not compact. Since $-(\theta(x) + \mu_a(x)) < 0$, $\forall x \in \Omega$, we use the similar arguments as in Lemma 4.4 and Lemma 4.5 of [13] (see also [22]) to show the following results.

Lemma 3.4. *Let $\lambda^* := s(\mathbf{B})$ be the spectral bound of \mathbf{B} .*

- (i) *If $\lambda^* \geq 0$, then λ^* is the principal eigenvalue of the eigenvalue problem (3.16) with a strongly positive eigenfunction.*
- (ii) *If $\lambda^* > 0$, then there is a small $\epsilon_0 > 0$ such that $\lambda_{\epsilon_0}^* > 0$, where $\lambda_{\epsilon_0}^*$ is the principal eigenvalue of the following eigenvalue problem*

$$\begin{cases} \lambda\psi_1(x) = k\delta(x) \left(1 - \frac{\epsilon_0}{C}\right) \psi_2(x) - (\theta(x) + \mu_a(x))\psi_1(x), & x \in \Omega, \\ \lambda\psi_2(x) = D_M\Delta\psi_2(x) + \theta(x)\psi_1(x) - \mu_m(x)\psi_2(x), & x \in \Omega, \\ \frac{\partial\psi_2(x)}{\partial\nu} = 0, & x \in \partial\Omega. \end{cases} \quad (3.17)$$

In the following, we shall adopt the results developed in [40, Section 3] (see also [39]) to define the mosquito reproduction number. To this end, we let

$$\mathbf{F}^M(x) = \begin{pmatrix} 0 & k\delta(x) \\ 0 & 0 \end{pmatrix}, \quad \mathbf{V}^M(x) = \begin{pmatrix} \theta(x) + \mu_a(x) & 0 \\ -\theta(x) & \mu_m(x) \end{pmatrix}. \quad (3.18)$$

Assume that $S^M(t) : C(\bar{\Omega}, \mathbb{R}^2) \rightarrow C(\bar{\Omega}, \mathbb{R}^2)$ be the C_0 -semigroup generated by the following system

$$\begin{pmatrix} \frac{\partial u_1}{\partial t} \\ \frac{\partial M}{\partial t} \end{pmatrix} = \begin{pmatrix} 0 \\ D_M\Delta M \end{pmatrix} - \mathbf{V}^M(x) \begin{pmatrix} u_1 \\ M \end{pmatrix}, \quad x \in \Omega, \quad t > 0,$$

with the boundary condition

$$\frac{\partial M}{\partial\nu} = 0, \quad x \in \partial\Omega, \quad t > 0.$$

In order to define the mosquito reproduction number, we assume that both aquatic and susceptible female mosquito are near the state $(0, 0)$, and introduce initial fertile mosquitos at time $t = 0$ with the spatial distribution described by $\varphi \in C(\bar{\Omega}, \mathbb{R}^2)$. Then $S^M(t)\varphi$ represents the distribution of fertile individuals of female mosquito at time $t \geq 0$. Let $\mathbf{L}^M : C(\bar{\Omega}, \mathbb{R}^2) \rightarrow C(\bar{\Omega}, \mathbb{R}^2)$ be defined by

$$\mathbf{L}^M(\varphi)(\cdot) = \int_0^\infty \mathbf{F}^M(\cdot)(S^M(t)\varphi)(\cdot)dt.$$

Here $\mathbf{L}^M(\varphi)(\cdot)$ represents the distribution of the total new female mosquito population generated by initial fertile individuals of female mosquito, φ , and hence, \mathbf{L}^M is the next generation operator. We define the spectral radius of \mathbf{L}^M as the mosquito reproduction number, \mathcal{R}^M , that is,

$$\mathcal{R}^M := r(\mathbf{L}^M).$$

Let

$$\mathbb{Y}_C := \{(u_1^0, M^0) \in C(\bar{\Omega}, \mathbb{R}_+^2) : 0 \leq u_1^0(x) \leq C, \forall x \in \bar{\Omega}\}.$$

Lemma 3.5. *For any $(u_1^0(\cdot), M^0(\cdot)) \in \mathbb{Y}_C$, let $(u_1(\cdot, t), M(\cdot, t))$ be the solution of (3.8) with $(u_1(\cdot, 0), M(\cdot, 0)) = (u_1^0(\cdot), M^0(\cdot))$. If $\mathcal{R}^M > 1$ and $(u_1^0(\cdot), M^0(\cdot)) \neq (0, 0)$, then we have*

$$\lim_{t \rightarrow \infty} (u_1(x, t), M(x, t)) = (A^*(x), M_s^*(x)), \text{ uniformly for } x \in \bar{\Omega},$$

where $0 < A^*(x) < C$ and $M_s^*(x) > 0$, for all $x \in \bar{\Omega}$.

Proof. It can be shown that \mathbb{Y}_C is a positively invariant set for system (3.8), and hence, we may define the associated solution semiflow $\Phi(t) : \mathbb{Y}_C \rightarrow \mathbb{Y}_C$ by

$$\Phi(t)(u_1^0, M^0) = (u_1(\cdot, t, (u_1^0, M^0)), M(\cdot, t, (u_1^0, M^0))), \quad \forall t \geq 0, (u_1^0, M^0) \in \mathbb{Y}_C,$$

where $(u_1(\cdot, t, (u_1^0, M^0)), M(\cdot, t, (u_1^0, M^0)))$ is the solution of (3.8). Note that $\Phi(t)$ is monotone in \mathbb{Y}_C , and strongly monotone in the interior of \mathbb{Y}_C . Also, we can show that $u_1(x, t) < C$, for all $x \in \bar{\Omega}$ and $t > 0$. The first equation of (3.8) has no diffusion term, and hence, the associated solution semiflow $\Phi(t)$ is not compact. Since $-(\theta(x) + \mu_a(x)) < 0$, $\forall x \in \bar{\Omega}$, we can use simple comparison arguments together with similar arguments in [13, Theorem 4.1] (see also [12, Lemma 4.1] and [20, Theorem 2.6]) to overcome this problem and then we can further show that $\Phi(t)$ admits a global attractor on \mathbb{Y}_C .

By [40, Theorem 3.1] (see also [37, Theorem 3.5]), it follows that $\mathcal{R}^M - 1$ and $s(\mathbf{B})$ have the same sign, that is, $s(\mathbf{B}) > 0$. Then Lemma 3.4 implies that $\lambda^* := s(\mathbf{B}) > 0$ is the principal eigenvalue of (3.16) and there is a small $\epsilon_0 > 0$ such that $\lambda_{\epsilon_0}^* > 0$, where $\lambda_{\epsilon_0}^*$ is the principal eigenvalue of (3.17). Let

$$\mathbb{Y}_0 := \{(u_1^0, M^0) \in \mathbb{Y}_C : (u_1^0, M^0) \neq (0, 0)\}.$$

Then we can show that $(0, 0)$ is a uniform weak repeller for \mathbb{Y}_0 (see, e.g., [14, Theorem 2.1(ii)]) in the sense that

$$\limsup_{t \rightarrow \infty} \|\Phi(t)(u_1^0, M^0) - (0, 0)\| \geq \epsilon_0, \quad \forall (u_1^0, M^0) \in \mathbb{Y}_0.$$

By [46, Theorem 1.3.3], we can further show that $\Phi(t)$ is uniformly persistent with respect to $(\mathbb{Y}_0, \partial\mathbb{Y}_0)$ in the sense that there exists $\eta_0 > 0$ such that

$$\liminf_{t \rightarrow \infty} \|\Phi_t(u_1^0, M^0)\| \geq \eta_0, \quad \forall (u_1^0, M^0) \in \mathbb{Y}_0.$$

Using the arguments similar to those in [8, Theorem 2.2] with slight modifications, we can show that $\Phi(t)$ is strictly subhomogeneous in the sense that

$$\Phi(t)(\varsigma u_1^0, \varsigma M^0) > \varsigma \Phi(t)(u_1^0, M^0), \quad \forall (u_1^0, M^0) \gg 0, \varsigma \in (0, 1).$$

It then follows from [46, Theorem 2.3.2] (see also [12, Theorems 3.2]) that the conclusions in our theorem are valid. \square

In the following remark, we give some comments on the case $\mathcal{R}^M < 1$.

Remark 3.1. Due to the loss of compactness for system (3.15), we are unable to show that λ^* is the principal eigenvalue of the eigenvalue problem (3.16) when

$\mathcal{R}^M < 1$. Thus, it is mathematically difficult to show that the solution of (3.8), $(u_1(\cdot, t), M(\cdot, t))$, satisfies

$$\lim_{t \rightarrow \infty} (u_1(x, t), M(x, t)) = (0, 0), \text{ uniformly for } x \in \bar{\Omega}. \quad (3.19)$$

However, if all coefficients of system (3.15) are positive constants (independent of x , homogeneous environment), then we can use the same arguments as in [13, Lemma 3.3] to show that λ^* is the principal eigenvalue of (3.16), and then, a simple comparison argument leads to the conclusion that (3.19) holds if $\mathcal{R}^M < 1$.

3.2.2. Infection invasion threshold. Because of the spatial heterogeneity of temperature, the basic reproduction number, $\bar{\mathcal{R}}_0$, defined above can not provide threshold condition for dengue to persist in the case of heterogeneous environment. In this sub-section we formulate the infection invasion threshold, \mathcal{R}_0 , that describes the global dynamics of dengue persistence. We assume that $\mathcal{R}^M > 1$ asserting the instability of $E_0(x)$ and existence of $E_1(x)$. Linearizing system (3.1) at the disease-free steady-state $E_1(x)$, we get the following system for (u_3, u_4, u_6, u_7) components:

$$\begin{cases} \frac{\partial u_3}{\partial t} = D_M \Delta u_3 + \frac{b\beta_m(x)M_s^*(x)}{H(x)} u_7 - (\gamma_m(x) + \mu_m(x)) u_3, & x \in \Omega, t > 0, \\ \frac{\partial u_4}{\partial t} = D_M \Delta u_4 + \gamma_m(x) u_3 - \mu_m(x) u_4, & x \in \Omega, t > 0, \\ \frac{\partial u_6}{\partial t} = D_H \Delta u_6 + b\beta_h(x) u_4 - (\gamma_h + \mu_h) u_6, & x \in \Omega, t > 0, \\ \frac{\partial u_7}{\partial t} = D_H \Delta u_7 + \gamma_h u_6 - (\alpha_h + \mu_h) u_7, & x \in \Omega, t > 0, \\ \frac{\partial u_i}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, i = 3, 4, 6, 7. \end{cases} \quad (3.20)$$

Substituting $u_i(x, t) = e^{\Lambda t} \varphi_i(x)$, $i = 3, 4, 6, 7$, into (3.20), we get the following associated eigenvalue problem:

$$\begin{cases} \Lambda \varphi_3(x) = D_M \Delta \varphi_3 + \frac{b\beta_m(x)M_s^*(x)}{H(x)} \varphi_7 - (\gamma_m(x) + \mu_m(x)) \varphi_3, & x \in \Omega, \\ \Lambda \varphi_4(x) = D_M \Delta \varphi_4 + \gamma_m(x) \varphi_3 - \mu_m(x) \varphi_4, & x \in \Omega, \\ \Lambda \varphi_6(x) = D_H \Delta \varphi_6 + b\beta_h(x) \varphi_4 - (\gamma_h + \mu_h) \varphi_6, & x \in \Omega, \\ \Lambda \varphi_7(x) = D_H \Delta \varphi_7 + \gamma_h \varphi_6 - (\alpha_h + \mu_h) \varphi_7, & x \in \Omega, \\ \frac{\partial \varphi_i}{\partial \nu} = 0, & x \in \partial\Omega, i = 3, 4, 6, 7. \end{cases} \quad (3.21)$$

By a similar argument as in [31, Theorem 7.6.1], we have the following results.

Lemma 3.6. *The eigenvalue problem (3.21) admits a principal eigenvalue, denoted by Λ^* , which is associated with a strongly positive eigenfunction.*

In the following, we shall adopt the results developed in [40, Section 3] (see also [39]) to define the infection invasion threshold for system (3.1). From (3.20), we define

$$\mathbb{F}(x) = \begin{pmatrix} 0 & 0 & 0 & \frac{b\beta_m(x)M_s^*(x)}{H(x)} \\ 0 & 0 & 0 & 0 \\ 0 & b\beta_h(x) & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$\mathbb{V}(x) = \begin{pmatrix} \gamma_m(x) + \mu_m(x) & 0 & 0 & 0 \\ -\gamma_m(x) & \mu_m(x) & 0 & 0 \\ 0 & 0 & \gamma_h + \mu_h & 0 \\ 0 & 0 & -\gamma_h & \alpha_h + \mu_h \end{pmatrix}.$$

Let $u_I = (u_3, u_4, u_6, u_7)^T$, $D_I \Delta u_I = (D_M \Delta u_3, D_M \Delta u_4, D_H \Delta u_6, D_H \Delta u_7)^T$, and $\mathbb{S}(t) : C(\bar{\Omega}, \mathbb{R}^4) \rightarrow C(\bar{\Omega}, \mathbb{R}^4)$ be the C_0 -semigroup generated by the following system

$$\begin{cases} \frac{\partial u_I}{\partial t} = D_I \Delta u_I - \mathbb{V}(x)u_I, & x \in \Omega, t > 0, \\ \frac{\partial u_i}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, i = 3, 4, 6, 7. \end{cases} \quad (3.22)$$

We assume that the state variables are near the disease-free steady state $E_1(x)$ and the spatial distribution of initial infection is described by $\phi \in C(\bar{\Omega}, \mathbb{R}^4)$. Then $\mathbb{S}(t)\phi(x)$ represents the distribution of those infected members as time evolves, and hence, the distribution of new infection at time t is $\mathbb{F}(x)\mathbb{S}(t)\phi(x)$. Let $\mathbb{L} : C(\bar{\Omega}, \mathbb{R}^4) \rightarrow C(\bar{\Omega}, \mathbb{R}^4)$ be defined by

$$\mathbb{L}(\phi)(\cdot) = \int_0^\infty \mathbb{F}(\cdot)(\mathbb{S}(t)\phi)(\cdot) dt.$$

Here $\mathbb{L}(\phi)(\cdot)$ represents the distribution of total new infected individuals during their infection period, and hence, \mathbb{L} is the next generation operator. By the idea of next generation operators (see, e.g., [5, 38, 39]), we define the spectral radius of \mathbb{L} as the infection invasion threshold for system (3.1), that is,

$$\mathcal{R}_0 := r(\mathbb{L}).$$

By [40, Theorem 3.1] (see also [37, Theorem 3.5]), we have the following observation.

Lemma 3.7. $\mathcal{R}_0 - 1$ and Λ^* have the same sign.

Furthermore, by [40, Theorem 3.2], it can also be shown that \mathcal{R}_0 can be determined by a principal eigenvalue of the elliptic eigenvalue problem, as stated in the following lemma.

Lemma 3.8. Consider the eigenvalue problem

$$\begin{cases} -D_I \Delta \varphi_I + \mathbb{V}(x)\varphi_I = \xi \mathbb{F}(x)\varphi_I, & x \in \Omega, \\ \frac{\partial \varphi_I}{\partial \nu} = 0, & x \in \partial\Omega, \end{cases} \quad (3.23)$$

where $\varphi_I = (\varphi_3, \varphi_4, \varphi_6, \varphi_7)^T$, $D_I \Delta \varphi_I = (D_M \Delta \varphi_3, D_M \Delta \varphi_4, D_H \Delta \varphi_6, D_H \Delta \varphi_7)^T$, and $\frac{\partial \varphi_I}{\partial \nu} = (\frac{\partial \varphi_3}{\partial \nu}, \frac{\partial \varphi_4}{\partial \nu}, \frac{\partial \varphi_6}{\partial \nu}, \frac{\partial \varphi_7}{\partial \nu})^T$. If system (3.23) admits a unique positive eigenvalue ξ_0 with a positive eigenfunction, then $\mathcal{R}_0 = \frac{1}{\xi_0}$.

We next prove that the infection invasion threshold \mathcal{R}_0 can describe the global dynamics of system (3.1), providing the condition whether the disease dies out ($\mathcal{R}_0 < 1$) or persists ($\mathcal{R}_0 > 1$). For this, we first prove the following lemma that will play an important role in establishing the persistence of (3.1).

Lemma 3.9. Suppose $u(x, t, \phi)$ is the solution of system (3.1) with $u(\cdot, 0, \phi) = \phi \in \mathbb{X}_C$.

(i) If $\phi_i(\cdot) \not\equiv 0$, for $i = 1, 2, 4$, then

$$u_i(x, t, \phi) > 0, \text{ for } x \in \bar{\Omega}, t > 0, \text{ and } 1 \leq i \leq 8. \quad (3.24)$$

(ii) If $\phi_i(\cdot) \not\equiv 0$, for $i = 1, 2, 4$, and $\mathcal{R}^M > 1$, then there exists $\sigma_0 > 0$ such that

$$\liminf_{t \rightarrow \infty} u_i(x, t, \phi) \geq \sigma_0, \text{ uniformly for } x \in \bar{\Omega}, \text{ and } i = 1, 2, 5. \quad (3.25)$$

(iii) Assume that $\phi_i(\cdot) \not\equiv 0$, for $i = 1, 2, 4$, and $\mathcal{R}^M > 1$. If there exists a $\sigma_1 > 0$ such that

$$\liminf_{t \rightarrow \infty} u_4(x, t, \phi) \geq \sigma_1, \text{ uniformly for } x \in \bar{\Omega}, \quad (3.26)$$

then there exists a $\sigma > 0$ such that

$$\liminf_{t \rightarrow \infty} u_i(x, t, \phi) \geq \sigma, \text{ uniformly for } x \in \bar{\Omega}, \text{ and } 1 \leq i \leq 8. \quad (3.27)$$

Proof. Part(i). Obviously, (3.24) holds for the case where $i = 5$. By the positivity of solutions (see Lemma 3.1) and the fourth equation of (3.1), we get

$$\begin{cases} \frac{\partial u_4}{\partial t} \geq D_M \Delta u_4 - \mu_m(x) u_4, & x \in \Omega, t > 0, \\ \frac{\partial u_4}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (3.28)$$

Since $\phi_4(\cdot) \not\equiv 0$, it follows from (3.28), the strong maximum principle (see, e. g., [28, p. 172, Theorem 4]) and the Hopf boundary lemma (see, e.g., [28, p. 170, Theorem 3]) that

$$u_4(x, t, \phi) > 0, \text{ for } x \in \bar{\Omega}, t > 0. \quad (3.29)$$

Claim 1.

$$u_6(x, t, \phi) > 0, \text{ for } x \in \bar{\Omega}, t > 0. \quad (3.30)$$

From the positivity of solutions and the sixth equation of (3.1), it follows that

$$\begin{cases} \frac{\partial u_6}{\partial t} \geq D_H \Delta u_6 - (\gamma_h + \mu_h) u_6, & x \in \Omega, t > 0, \\ \frac{\partial u_6}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (3.31)$$

Suppose, by contradiction, there exists $x_6 \in \bar{\Omega}$ and $t_6 > 0$ such that $u_6(x_6, t_6, \phi) = 0$. For the case where $x_6 \in \partial\Omega$, we apply the Hopf boundary lemma and get $\frac{\partial u_6(x_6, t_6, \phi)}{\partial \nu} < 0$, which is impossible. For the case where $x_6 \in \Omega$, we apply the strong maximum principle ([28, p. 174, Theorem 7]), we obtain that

$$u_6(x, t, \phi) \equiv 0, \forall x \in \bar{\Omega}, t \leq t_6. \quad (3.32)$$

From (3.32) and the sixth equation of (3.1), it follows that

$$u_5(x, t, \phi) u_4(x, t, \phi) \equiv 0, \forall x \in \bar{\Omega}, t \leq t_6, \quad (3.33)$$

which contradicts either the fifth equation of (3.1) or (3.29). Thus, Claim 1 is proved.

By (3.30) and the similar arguments to those in Claim 1, we can conclude that (3.24) holds for the cases where $i = 7$, $i = 8$ and $i = 3$. Since $\phi_2(\cdot) \not\equiv 0$, it follows from the strong maximum principle and the Hopf boundary lemma that (3.24) holds for the case where $i = 2$. Next, we prove that (3.24) holds for the case where $i = 1$. Suppose, by contradiction, there exists $x_1 \in \bar{\Omega}$ and $t_1 > 0$ such that $u_1(x_1, t_1, \phi) = 0$. Then it follows from the first equation of (3.1) that

$$0 = \frac{\partial u_1(x_1, t_1, \phi)}{\partial t} = k\delta(x_1)[u_2(x_1, t_1, \phi) + u_3(x_1, t_1, \phi) + u_4(x_1, t_1, \phi)],$$

which implies that $u_2(x_1, t_1, \phi) = 0$, a contradiction. Thus, we complete the proof of Part (i).

Part(ii). Recall that $M(x, t) = u_2(x, t) + u_3(x, t) + u_4(x, t)$ is defined in (3.7), and $(u_1(x, t), M(x, t))$ satisfies system (3.8) with $(u_1(\cdot, 0), M(\cdot, 0)) = (\phi_1(\cdot), \phi_2(\cdot) +$

$\phi_3(\cdot) + \phi_4(\cdot) \not\equiv (0, 0)$. Since $(u_1(\cdot, 0), M(\cdot, 0)) \not\equiv (0, 0)$ and $\mathcal{R}^M > 1$, it follows from Lemma 3.5 that

$$\lim_{t \rightarrow \infty} (u_1(x, t), M(x, t)) = (A^*(x), M_s^*(x)), \text{ uniformly for } x \in \bar{\Omega}.$$

For any $g \in C(\bar{\Omega}, \mathbb{R})$, we define $\bar{g} = \max_{x \in \bar{\Omega}} g(x)$, $\hat{g} = \min_{x \in \bar{\Omega}} g(x)$. Then there exists $\tau_1 > 0$ such that

$$u_1(x, t) \geq \frac{1}{2}A^*(x) \geq \frac{1}{2}\hat{A}, \quad u_4(x, t) \leq M(x, t) \leq 2M_s^*(x) \leq 2\overline{M_s}, \quad \forall x \in \bar{\Omega}, \quad t \geq \tau_1. \quad (3.34)$$

In view of (3.4) and (3.6), it follows that there exists $\tau_2 \geq \tau_1$ such that

$$\hat{H}/2 \leq N_H(x, t) \leq 2\overline{H}, \quad \forall x \in \bar{\Omega}, \quad t \geq \tau_2. \quad (3.35)$$

From (3.34) and the second equation of system (3.1), we have

$$\begin{cases} \frac{\partial u_2}{\partial t} \geq D_M \Delta u_2 + \frac{1}{2}\hat{\theta} \hat{A} - [b\overline{\beta_m} + \overline{\mu_m}]u_2, & x \in \Omega, \quad t \geq \tau_1, \\ \frac{\partial u_2}{\partial \nu} = 0, & x \in \partial\Omega, \quad t \geq \tau_1, \end{cases} \quad (3.36)$$

where we have used the fact that $\frac{u_5}{u_5+u_6+u_7+u_8} \leq 1$. Applying the standard parabolic comparison theorem (see, e.g., [31, Theorem 7.3.4]) and Lemma 3.2 again, we obtain

$$\liminf_{t \rightarrow \infty} u_2(x, t) \geq L_2 := \frac{\frac{1}{2}\hat{\theta} \hat{A}}{b\overline{\beta_m} + \overline{\mu_m}}, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.37)$$

From (3.34), (3.35) and the fifth equation of system (3.1), we have

$$\begin{cases} \frac{\partial u_5}{\partial t} \geq D_H \Delta u_5 + \hat{\Lambda}_h - [\mu_h + \frac{2b\overline{\beta_h} \overline{M_s}}{\hat{H}/2}]u_5, & x \in \Omega, \quad t \geq \tau_2, \\ \frac{\partial u_5}{\partial \nu} = 0, & x \in \partial\Omega, \quad t \geq \tau_2. \end{cases} \quad (3.38)$$

By the standard parabolic comparison theorem (see, e.g., [31, Theorem 7.3.4]) and Lemma 3.2, we obtain

$$\liminf_{t \rightarrow \infty} u_5(x, t) \geq L_5 := \frac{\hat{\Lambda}_h}{\mu_h + \frac{4b\overline{\beta_h} \overline{M_s}}{\hat{H}}}, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.39)$$

By (3.34), (3.39), and (3.37), the proof of Part (ii) is complete.

Part(iii). By (3.25) and (3.26), it suffices to show that (3.27) holds for $i = 3, 6, 7, 8$. From (3.26), (3.39) and (3.37), there exists $\tau_3 \geq \tau_2$ such that

$$u_4(x, t) \geq \frac{1}{2}\sigma_1, \quad u_5(x, t) \geq \frac{1}{2}L_5, \quad \text{and } u_2(x, t) \geq \frac{1}{2}L_2, \quad \forall x \in \bar{\Omega}, \quad t \geq \tau_3. \quad (3.40)$$

From (3.35), (3.40) and the sixth equation of system (3.1), we have

$$\begin{cases} \frac{\partial u_6}{\partial t} \geq D_H \Delta u_6 + \frac{b\hat{\beta}_h L_5 \sigma_1}{8\hat{H}} - (\gamma_h + \mu_h)u_6, & x \in \Omega, \quad t \geq \tau_3, \\ \frac{\partial u_6}{\partial \nu} = 0, & x \in \partial\Omega, \quad t \geq \tau_3. \end{cases} \quad (3.41)$$

Applying the standard parabolic comparison theorem (see, e.g., [31, Theorem 7.3.4]) and Lemma 3.2, we obtain

$$\liminf_{t \rightarrow \infty} u_6(x, t) \geq L_6 := \frac{b\hat{\beta}_h L_5 \sigma_1}{8\hat{H}(\gamma_h + \mu_h)}, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.42)$$

By (3.42), there exists $\tau_4 \geq \tau_3$ such that

$$u_6(x, t) \geq \frac{1}{2}L_6, \quad \forall x \in \bar{\Omega}, \quad t \geq \tau_4. \quad (3.43)$$

From (3.43) and the seventh equation of system (3.1), we have

$$\begin{cases} \frac{\partial u_7}{\partial t} \geq D_H \Delta u_7 + \frac{1}{2} \gamma_h L_6 - (\alpha_h + \mu_h) u_7, & x \in \Omega, t \geq \tau_4, \\ \frac{\partial u_7}{\partial \nu} = 0, & x \in \partial\Omega, t \geq \tau_4. \end{cases} \quad (3.44)$$

Then

$$\liminf_{t \rightarrow \infty} u_7(x, t) \geq L_7 := \frac{\gamma_h L_6}{2(\alpha_h + \mu_h)}, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.45)$$

By (3.45), there exists $\tau_5 \geq \tau_4$ such that

$$u_7(x, t) \geq \frac{1}{2} L_7, \quad \forall x \in \bar{\Omega}, t \geq \tau_5. \quad (3.46)$$

In view of (3.46) and the last equation of system (3.1), we have

$$\begin{cases} \frac{\partial u_8}{\partial t} \geq D_H \Delta u_8 + \frac{1}{2} \alpha_h L_7 - \mu_h u_8, & x \in \Omega, t \geq \tau_5, \\ \frac{\partial u_8}{\partial \nu} = 0, & x \in \partial\Omega, t \geq \tau_5. \end{cases} \quad (3.47)$$

Then

$$\liminf_{t \rightarrow \infty} u_8(x, t) \geq L_8 := \frac{\alpha_h L_7}{2\mu_h}, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.48)$$

By (3.35), (3.40), (3.46), and the third equation of system (3.1), it follows that

$$\begin{cases} \frac{\partial u_3}{\partial t} \geq D_M \Delta u_3 + \frac{b\widehat{\beta}_m L_2 L_7}{8\widehat{H}} - (\overline{\gamma}_m + \overline{\mu}_m) u_3, & x \in \Omega, t \geq \tau_5, \\ \frac{\partial u_3}{\partial \nu} = 0, & x \in \partial\Omega, t \geq \tau_5. \end{cases} \quad (3.49)$$

Then

$$\liminf_{t \rightarrow \infty} u_3(x, t) \geq L_3 := \frac{b\widehat{\beta}_m L_2 L_7}{8\widehat{H}(\overline{\gamma}_m + \overline{\mu}_m)}, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.50)$$

From (3.42), (3.45), (3.48), and (3.50), we complete the proof of Part (iii). \square

As mentioned earlier, we prove in the following theorem that dengue dynamics can be globally described by the infection invasion threshold \mathcal{R}_0 :

Theorem 3.1. *Suppose $u(x, t, \phi)$ is the solution of system (3.1) with $u(\cdot, 0, \phi) = \phi \in \mathbb{X}_C$, where \mathbb{X}_C is given in (3.2). Assume that $\mathcal{R}^M > 1$. Then the following statements hold.*

- (i) *If $\mathcal{R}_0 < 1$, then the disease-free steady state $E_1(x)$ is globally attractive in the sense that if $(\phi_1(\cdot), \phi_2(\cdot)) \neq (0, 0)$, we have*

$$\lim_{t \rightarrow \infty} u(x, t, \phi) = E_1(x), \text{ uniformly for all } x \in \bar{\Omega}.$$

- (ii) *If $\mathcal{R}_0 > 1$, then system (3.1) admits at least one (componentwise) positive steady state $\hat{u}(x)$ and there exists a $\sigma > 0$ such that for any $\phi \in \mathbb{X}_C$ with $\phi_i(\cdot) \neq 0, \forall i = 1, 2, 4$, we have*

$$\liminf_{t \rightarrow \infty} u_i(x, t) \geq \sigma, \text{ uniformly for all } x \in \bar{\Omega}, \forall 1 \leq i \leq 8.$$

Proof. Part (i). We first assume that $\mathcal{R}_0 < 1$. It then follows from Lemma 3.7 that $\Lambda^* < 0$. By the continuity, there is an $\epsilon_1 > 0$ such that $\Lambda_{\epsilon_1}^* < 0$, where $\Lambda_{\epsilon_1}^*$ is the principal eigenvalue of

$$\begin{cases} \Lambda\varphi_3(x) = D_M\Delta\varphi_3 + \frac{b\beta_m(x)[M_s^*(x)+\epsilon_1]}{H(x)}\varphi_7 - (\gamma_m(x) + \mu_m(x))\varphi_3, & x \in \Omega, \\ \Lambda\varphi_4(x) = D_M\Delta\varphi_4 + \gamma_m(x)\varphi_3 - \mu_m(x)\varphi_4, & x \in \Omega, \\ \Lambda\varphi_6(x) = D_H\Delta\varphi_6 + \frac{b\beta_h(x)[H+\epsilon_1]}{H(x)}\varphi_4 - (\gamma_h + \mu_h)\varphi_6, & x \in \Omega, \\ \Lambda\varphi_7(x) = D_H\Delta\varphi_7 + \gamma_h\varphi_6 - (\alpha_h + \mu_h)\varphi_7, & x \in \Omega, \\ \frac{\partial\varphi_i}{\partial\nu} = 0, & x \in \partial\Omega, \quad i = 3, 4, 6, 7. \end{cases} \quad (3.51)$$

By the positivity of solutions, (3.4), (3.6), (3.7), and Lemma 3.5, it follows that there is a $t_1 := t_1(\phi)$ such that

$$\begin{aligned} u_2(x, t, \phi) &\leq M_s^*(x) + \epsilon_1, \quad u_5(x, t, \phi) \leq H(x) + \epsilon_1, \quad N_H(x, t, \phi) \geq H(x) - \epsilon_1, \\ &\forall t \geq t_1, \quad x \in \bar{\Omega}. \end{aligned}$$

From the third, fourth, sixth, and seventh equations of system (3.1), it follows that

$$\begin{cases} \frac{\partial u_3}{\partial t} \leq D_M\Delta u_3 + \frac{b\beta_m(x)[M_s^*(x)+\epsilon_1]}{H(x)-\epsilon_1}u_7 - (\gamma_m(x) + \mu_m(x))u_3, & x \in \Omega, \quad t \geq t_1, \\ \frac{\partial u_4}{\partial t} = D_M\Delta u_4 + \gamma_m(x)u_3 - \mu_m(x)u_4, & x \in \Omega, \quad t \geq t_1, \\ \frac{\partial u_6}{\partial t} \leq D_H\Delta u_6 + \frac{b\beta_h(x)[H+\epsilon_1]}{H(x)-\epsilon_1}u_4 - (\gamma_h + \mu_h)u_6, & x \in \Omega, \quad t \geq t_1, \\ \frac{\partial u_7}{\partial t} = D_H\Delta u_7 + \gamma_h u_6 - (\alpha_h + \mu_h)u_7, & x \in \Omega, \quad t \geq t_1, \\ \frac{\partial u_i}{\partial\nu} = 0, & x \in \partial\Omega, \quad t \geq t_1, \quad i = 3, 4, 6, 7. \end{cases} \quad (3.52)$$

We may assume that $\varphi_I^{\epsilon_1}(x) := (\varphi_3^{\epsilon_1}(x), \varphi_4^{\epsilon_1}(x), \varphi_6^{\epsilon_1}(x), \varphi_7^{\epsilon_1}(x))$ is a strongly positive eigenfunction corresponding to $\Lambda_{\epsilon_1}^*$ (see also Lemma 3.6). For any given $\phi \in \mathbb{X}_C$, there exists some $\zeta > 0$ such that

$$(u_3(x, t_1, \phi), u_4(x, t_1, \phi), u_6(x, t_1, \phi), u_7(x, t_1, \phi)) \leq \zeta\varphi_I^{\epsilon_1}(x), \quad \forall x \in \bar{\Omega}.$$

The comparison principle implies that

$$(u_3(x, t, \phi), u_4(x, t, \phi), u_6(x, t, \phi), u_7(x, t, \phi)) \leq \zeta e^{\Lambda_{\epsilon_1}^*(t-t_1)}\varphi_I^{\epsilon_1}(x), \quad \forall x \in \bar{\Omega}, \quad t \geq t_1,$$

and it then follows that $\lim_{t \rightarrow \infty} (u_3(x, t, \phi), u_4(x, t, \phi), u_6(x, t, \phi), u_7(x, t, \phi)) = 0$ uniformly for $x \in \bar{\Omega}$. Then the equation u_5 in (3.1) is asymptotic to system (3.5), and hence, it follows from Lemma 3.2 and the theory for asymptotically autonomous semiflows (see, e.g., [36, Corollary 4.3]) that

$$\lim_{t \rightarrow \infty} u_5(x, t) = H(x) \text{ uniformly in } x \in \bar{\Omega}.$$

Similarly, the equations (u_1, u_2) in (3.1) are asymptotic to system (3.8), and it follows from Lemma 3.5 and [36, Corollary 4.3] that

$$\lim_{t \rightarrow \infty} (u_1(x, t), u_2(x, t)) = (A^*(x), M_s^*(x)), \text{ uniformly for } x \in \bar{\Omega}. \quad (3.53)$$

Thus, Part (i) is proved.

We are ready to prove Part (ii). Let

$$\mathbb{W}_0 = \{\phi \in \mathbb{X}_C : \phi_1(\cdot) \not\equiv 0, \phi_2(\cdot) \not\equiv 0 \text{ and } \phi_4(\cdot) \not\equiv 0\},$$

and

$$\partial\mathbb{W}_0 = \mathbb{X}_C \setminus \mathbb{W}_0 = \{\phi \in \mathbb{X}_C : \phi_1(\cdot) \equiv 0 \text{ or } \phi_2(\cdot) \equiv 0 \text{ or } \phi_4(\cdot) \equiv 0\}.$$

Recall that $\Psi(t) : \mathbb{X}_C \rightarrow \mathbb{X}_C$ is the solution semiflows associated with system (3.1). By Lemma 3.9, it follows that for any $\phi \in \mathbb{W}_0$, we have $u_i(x, t, \phi) > 0$, $\forall x \in \bar{\Omega}$, $t > 0$, $i = 1, 2, 4$. In other words, $\Psi(t)\mathbb{W}_0 \subseteq \mathbb{W}_0$, $\forall t \geq 0$. Let

$$M_\partial := \{\phi \in \partial\mathbb{W}_0 : \Psi(t)\phi \in \partial\mathbb{W}_0, \forall t \geq 0\},$$

and $\omega(\phi)$ be the omega limit set of the orbit $O^+(\phi) := \{\Psi(t)\phi : t \geq 0\}$.

Claim 1. $\omega(\psi) \subseteq \{E_0(x)\} \cup \{E_1(x)\}$, $\forall \psi \in M_\partial$.

Since $\psi \in M_\partial$, we have $\Psi(t)\psi \in \partial\mathbb{W}_0$, $\forall t \geq 0$, that is, $u_1(\cdot, t, \psi) \equiv 0$ or $u_2(\cdot, t, \psi) \equiv 0$ or $u_4(\cdot, t, \psi) \equiv 0$, $\forall t \geq 0$. In case where $u_4(\cdot, t, \psi) \equiv 0$, $\forall t \geq 0$. Then it follows from the fourth equation and the sixth equation of system (3.1) that $u_3(\cdot, t, \psi) \equiv 0$, $\forall t \geq 0$, and $u_6(\cdot, t, \psi)$ satisfies

$$\begin{cases} \frac{\partial u_6}{\partial t} = D_H \Delta u_6 - (\gamma_h + \mu_h)u_6, & x \in \Omega, t > 0, \\ \frac{\partial u_6}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, \end{cases}$$

and hence,

$$\lim_{t \rightarrow \infty} u_6(x, t, \psi) = 0, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.54)$$

In view of (3.54), the seventh equation of (3.1), and the theory for asymptotically autonomous semiflows (see, e.g., [36, Corollary 4.3]), we have

$$\lim_{t \rightarrow \infty} u_7(x, t, \psi) = 0, \text{ uniformly for } x \in \bar{\Omega}. \quad (3.55)$$

Similarly, (3.55) and the eighth equation of (3.1) imply that

$$\lim_{t \rightarrow \infty} u_8(x, t, \psi) = 0, \text{ uniformly for } x \in \bar{\Omega}.$$

The equations (u_1, u_2) in (3.1) are asymptotic to system (3.8), and hence, (3.53) is valid. Thus,

$$\lim_{t \rightarrow \infty} u(x, t, \psi) = E_1(x), \text{ uniformly for all } x \in \bar{\Omega}. \quad (3.56)$$

In case where $u_4(\cdot, \hat{t}_0, \psi) \not\equiv 0$, for some $\hat{t}_0 \geq 0$. Then we can show that $u_4(x, t, \psi) > 0$, for all $x \in \bar{\Omega}$ and $t > \hat{t}_0$, and hence, $u_1(\cdot, t, \psi) \equiv 0$ or $u_2(\cdot, t, \psi) \equiv 0$, for all $t > \hat{t}_0$. In case where $u_2(\cdot, t, \psi) \equiv 0$, for all $t > \hat{t}_0$. By the second equation of (3.1), we have $u_1(\cdot, t, \psi) \equiv 0$, for all $t > \hat{t}_0$. Then it is easy to show that

$$\lim_{t \rightarrow \infty} u(x, t, \psi) = E_0(x), \text{ uniformly for all } x \in \bar{\Omega}. \quad (3.57)$$

In case where $u_2(\cdot, \hat{t}_1, \psi) \not\equiv 0$, for some $\hat{t}_1 > \hat{t}_0$. Then we can show that $u_2(x, t, \psi) > 0$, for all $x \in \bar{\Omega}$ and $t > \hat{t}_1$, and hence, $u_1(\cdot, t, \psi) \equiv 0$, for all $t > \hat{t}_1$. On the other hand, we substitute $u_1(\cdot, t, \psi) \equiv 0$, $t > \hat{t}_1$ into the first equation of (3.1), and we get a contradiction that $u_2(\cdot, t, \psi) \equiv 0$, for all $t > \hat{t}_1$. Thus, this subcase cannot happen and Claim 1 is proved.

Since $\mathcal{R}_0 > 1$, it follows from Lemma 3.7 that $\Lambda^* > 0$. By continuity, there is an $\epsilon_2 > 0$ such that $\Lambda_{\epsilon_2}^* > 0$, where $\Lambda_{\epsilon_2}^*$ is the principal eigenvalue of

$$\begin{cases} \Lambda\varphi_3(x) = D_M\Delta\varphi_3 + \frac{b\beta_m(x)[M_s^*(x)-\epsilon_2]}{H(x)+4\epsilon_2}\varphi_7 - (\gamma_m(x) + \mu_m(x))\varphi_3, & x \in \Omega, \\ \Lambda\varphi_4(x) = D_M\Delta\varphi_4 + \gamma_m(x)\varphi_3 - \mu_m(x)\varphi_4, & x \in \Omega, \\ \Lambda\varphi_6(x) = D_H\Delta\varphi_6 + \frac{b\beta_h(x)[H-\epsilon_2]}{H(x)+4\epsilon_2}\varphi_4 - (\gamma_h + \mu_h)\varphi_6, & x \in \Omega, \\ \Lambda\varphi_7(x) = D_H\Delta\varphi_7 + \gamma_h\varphi_6 - (\alpha_h + \mu_h)\varphi_7, & x \in \Omega, \\ \frac{\partial\varphi_i}{\partial\nu} = 0, & x \in \partial\Omega, \quad i = 3, 4, 6, 7. \end{cases} \quad (3.58)$$

Claim 2. $E_1(x)$ is a uniform weak repeller for \mathbb{W}_0 in the sense that

$$\limsup_{t \rightarrow \infty} \|\Psi(t)\phi - E_1(x)\| \geq \epsilon_2, \quad \forall \phi \in \mathbb{W}_0.$$

Suppose, by contradiction, there exists $\phi_0 \in \mathbb{W}_0$ such that

$$\limsup_{t \rightarrow \infty} \|\Psi(t)\phi_0 - E_1(x)\| < \epsilon_2.$$

Then there exists $t_2 > 0$ such that for all $t \geq t_2$, $x \in \bar{\Omega}$, we have

$$\begin{aligned} u_2(x, t, \phi_0) &> M_s^*(x) - \epsilon_2, \quad H(x) + \epsilon_2 > u_5(x, t, \phi_0) > H(x) - \epsilon_2, \\ &\text{and } H(x) + 4\epsilon_2 > N_H(x, t, \phi_0). \end{aligned}$$

From the third, fourth, sixth, and seventh equations of system (3.1), it follows that

$$\begin{cases} \frac{\partial u_3}{\partial t} \geq D_M\Delta u_3 + \frac{b\beta_m(x)[M_s^*(x)-\epsilon_2]}{H(x)+4\epsilon_2}u_7 - (\gamma_m(x) + \mu_m(x))u_3, & x \in \Omega, \quad t \geq t_2, \\ \frac{\partial u_4}{\partial t} = D_M\Delta u_4 + \gamma_m(x)u_3 - \mu_m(x)u_4, & x \in \Omega, \quad t \geq t_2, \\ \frac{\partial u_6}{\partial t} \geq D_H\Delta u_6 + \frac{b\beta_h(x)[H-\epsilon_2]}{H(x)+4\epsilon_2}u_4 - (\gamma_h + \mu_h)u_6, & x \in \Omega, \quad t \geq t_2, \\ \frac{\partial u_7}{\partial t} = D_H\Delta u_7 + \gamma_h u_6 - (\alpha_h + \mu_h)u_7, & x \in \Omega, \quad t \geq t_2, \\ \frac{\partial u_i}{\partial\nu} = 0, & x \in \partial\Omega, \quad t \geq t_2, \quad i = 3, 4, 6, 7. \end{cases} \quad (3.59)$$

Since $\phi_0 \in \mathbb{W}_0$, it follows from Lemma 3.9 (i) that $u_i(x, t_2, \phi_0) > 0$, for all $x \in \bar{\Omega}$, $i = 3, 4, 6, 7$. Then there exists some $\zeta_2 > 0$ such that

$$(u_3(x, t_2, \phi_0), u_4(x, t_2, \phi_0), u_6(x, t_2, \phi_0), u_7(x, t_2, \phi_0)) \geq \zeta_2 \varphi_I^{\epsilon_2}(x), \quad \forall x \in \bar{\Omega},$$

where $\varphi_I^{\epsilon_2}(x) := (\varphi_3^{\epsilon_2}(x), \varphi_4^{\epsilon_2}(x), \varphi_6^{\epsilon_2}(x), \varphi_7^{\epsilon_2}(x))$ is a strongly positive eigenfunction corresponding to $\Lambda_{\epsilon_2}^*$. The comparison principle implies that

$$\begin{aligned} (u_3(x, t, \phi_0), u_4(x, t, \phi_0), u_6(x, t, \phi_0), u_7(x, t, \phi_0)) &\geq \zeta_2 e^{\Lambda_{\epsilon_2}^*(t-t_2)} \varphi_I^{\epsilon_2}(x), \\ &\forall x \in \bar{\Omega}, \quad t \geq t_2. \end{aligned}$$

Since $\Lambda_{\epsilon_2}^* > 0$, it follows that $u_i(x, t, \phi_0)$, $i = 3, 4, 5, 7$, is unbounded. This contradiction proves the Claim 2.

Since $\mathcal{R}^M > 1$, it follows from [40, Theorem 3.1] (see also [37, Theorem 3.5]) that $s(\mathbf{B}) > 0$, where $s(\mathbf{B})$ is given in Lemma 3.4. By the similar arguments in Lemma 4.4 and Lemma 4.5 of [13] (see also [22] and Lemma 3.4), we can deduce that $\lambda^* := s(\mathbf{B}) > 0$ is the principal eigenvalue of (3.16), and there is a small $\epsilon_3 > 0$ such that $\lambda_{\epsilon_3}^* > 0$, where $\lambda_{\epsilon_3}^*$ is the principal eigenvalue of the following eigenvalue problem

$$\begin{cases} \lambda\psi_1(x) = k\delta(x) \left(1 - \frac{\epsilon_3}{C}\right) \psi_2(x) - (\theta(x) + \mu_a(x))\psi_1(x), & x \in \Omega, \\ \lambda\psi_2(x) = D_M\Delta\psi_2(x) + \theta(x)\psi_1(x) - \left[\frac{b\beta_m(x)\epsilon_3}{H(x)-\epsilon_3} + \mu_m(x)\right]\psi_2(x), & x \in \Omega, \\ \frac{\partial\psi_2(x)}{\partial\nu} = 0, & x \in \partial\Omega. \end{cases} \quad (3.60)$$

Then we can use the similar arguments in Claim 2 to show the following result:
Claim 3. $E_0(x)$ is a uniform weak repeller for \mathbb{W}_0 in the sense that

$$\limsup_{t \rightarrow \infty} \|\Psi(t)\phi - E_0(x)\| \geq \epsilon_3, \quad \forall \phi \in \mathbb{W}_0.$$

Define a continuous function $p : \mathbb{X}_C \rightarrow [0, \infty)$ by

$$p(\phi) := \min\left\{\min_{x \in \Omega} \phi_1(x), \min_{x \in \Omega} \phi_2(x), \min_{x \in \Omega} \phi_4(x)\right\}, \quad \forall \phi \in \mathbb{X}_C.$$

By Lemma 3.9 (i), it follows that $p^{-1}(0, \infty) \subseteq \mathbb{W}_0$ and p has the property that if $p(\phi) > 0$ or $\phi \in \mathbb{W}_0$ with $p(\phi) = 0$, then $p(\Psi(t)\phi) > 0$, $\forall t > 0$. That is, p is a generalized distance function for the semiflow $\Psi(t) : \mathbb{X}_C \rightarrow \mathbb{X}_C$ (see, e.g., [32]). From the above claims, it follows that any forward orbit of $\Psi(t)$ in M_∂ converges to $\{E_0(x)\} \cup \{E_1(x)\}$. For $i = 0, 1$, $\{E_i(x)\}$ is isolated in \mathbb{X}_C and $W^s(\{E_i(x)\}) \cap \mathbb{W}_0 = \emptyset$, where $W^s(\{E_i(x)\})$ is the stable set of $\{E_i(x)\}$ (see [32]). It is obvious that no subset of $\{E_0(x)\} \cup \{E_1(x)\}$ forms a cycle in $\partial\mathbb{W}_0$. By Lemma 3.3, the semiflow $\Psi(t) : \mathbb{X}_C \rightarrow \mathbb{X}_C$ has a global compact attractor in \mathbb{X}_C , $\forall t \geq 0$. Then it follows from [32, Theorem 3] that there exists a $\sigma_1 > 0$ such that

$$\min_{\psi \in \omega(\phi)} p(\psi) > \sigma_1, \quad \forall \phi \in \mathbb{W}_0.$$

Hence, $\liminf_{t \rightarrow \infty} u_4(\cdot, t, \phi) \geq \sigma_1$, $\forall \phi \in \mathbb{W}_0$. From Lemma 3.9 (iii), there exists a $\sigma > 0$ such that

$$\liminf_{t \rightarrow \infty} u_i(\cdot, t, \phi) \geq \sigma, \quad \forall \phi \in \mathbb{W}_0, \quad 1 \leq i \leq 8.$$

Hence, the uniform persistence stated in the conclusion (ii) hold. By [20, Theorem 3.7 and Remark 3.10], it follows that $\Psi(t) : \mathbb{W}_0 \rightarrow \mathbb{W}_0$ has a global attractor A_0 . Using [20, Theorem 4.7], we deduce that $\Psi(t)$ admits a steady-state $\tilde{u}(\cdot) \in \mathbb{W}_0$. By Lemma 3.9 (i), we can further conclude that $\tilde{u}(\cdot)$ is a positive steady state of (3.1). We complete the proof of Part (ii). \square

4. Simulation results. For simplicity we consider $\Omega = [0, L] \subset \mathbb{R}$. Furthermore, we can take $L = 1$ by transforming $D_H \rightarrow D_H/L^2$, $D_M \rightarrow D_M/L^2$, and $T(x) \rightarrow T(xL)$. For illustration purposes, we consider a linearly decay function for temperature, $T(x)$, to represent a spatial variation of the environmental temperature. $T(0) = T_0$ and $T(1) = T_1$ stand for temperatures of a warmer place and a cooler place, respectively, while temperature in between is given by $T(x) = (T_1 - T_0)x + T_0$. An explicit expression for $\Lambda_h(x)$ is not available. To approximate $\Lambda_h(x)$, we assume that the human populations without infection and mobility remain constant, and take $\Lambda(x) = \mu_h(H_s + H_e + H_i + H_r)$ for the purpose of model simulation.

4.1. Solution methodology. We obtain solutions of the system (3.1) using finite element method. We assume that an affine family of simplicial triangulations $\{\mathcal{T}_h\}$ is given for Ω and define

$$\mathbb{U} = \{\mathbf{v} = (v_1, \dots, v_8)^T, v_i \in H^1(\Omega), i = 1, \dots, 8\}.$$

We denote the linear finite element space associated with \mathcal{T}_h by \mathbb{U}^h and $(u_1^h, \dots, u_8^h)^T$ by \mathbf{u}^h . Since the test functions v_i^h ($i = 1, \dots, 8$) in the weak formulation are linearly

independent of each other, a linear finite element solution $\mathbf{u}^h(t) \in \mathbb{U}^h$, $t \in (0, t_f]$ for the system (3.1) is defined by the weak formulation in the vector form as follows.

$$\int_{\Omega} (\mathbf{v}^h)^T \frac{\partial \mathbf{u}^h}{\partial t} dx + \int_{\Omega} \left(\frac{d\mathbf{v}^h}{dx} \right)^T \left(\mathbb{D} \frac{\partial \mathbf{u}^h}{\partial x} \right) dx = \int_{\Omega} (\mathbf{v}^h)^T \mathbf{f}(\mathbf{u}^h) dx, \quad \forall \mathbf{v}^h \in \mathbb{U}^h, \quad (4.1)$$

where $\mathbb{D} = \text{diag}(0, D_M, D_M, D_M, D_H, D_H, D_H, D_H)$ and \mathbf{f} denotes the right-hand-side functions of (3.1) except diffusion terms.

Let N_e and $N_v = N_e + 1$ denote the number of the elements and vertices of \mathcal{T}_h , respectively, and ϕ_j be the linear basis function associated with the j -th vertex, x_j . Then we can express the solution \mathbf{u}^h as

$$\mathbf{u}^h = \sum_{j=1}^{N_v} \mathbf{u}^j(t) \phi_j(x). \quad (4.2)$$

Denote the unknown vector as

$$\mathbf{U} = \left(u_1^1, \dots, u_8^1, u_1^2, \dots, u_8^2, \dots, \dots, u_1^{N_v}, \dots, u_8^{N_v} \right)^T. \quad (4.3)$$

Inserting (4.2) into (4.1) and taking $\mathbf{v}^h = \phi_j \mathbf{e}_i$ ($i = 1, \dots, 8$, $j = 1, \dots, N_v$) successively, we obtain the matrix form of the semi-discrete system as

$$\mathbf{M} \frac{d\mathbf{U}}{dt} + \mathbf{A} \mathbf{U} = \mathbf{F}(\mathbf{u}^h), \quad (4.4)$$

where \mathbf{M} and \mathbf{A} are the mass and stiffness matrices, respectively. Denote the matrix of basis functions as

$$\mathbf{\Phi} = [\phi_1 \mathbf{I}_8, \dots, \phi_{N_v} \mathbf{I}_8] \quad (4.5)$$

where \mathbf{I}_8 is the identity matrix of size 8. Then the matrices \mathbf{M} and \mathbf{A} , each of size $8N_v \times 8N_v$, are given by

$$\mathbf{M} = \int_{\Omega} \mathbf{\Phi}^T \mathbf{\Phi} dx, \quad \mathbf{A} = \int_{\Omega} \frac{d\mathbf{\Phi}^T}{dx} \left(\mathbb{D} \frac{d\mathbf{\Phi}}{dx} \right) dx. \quad (4.6)$$

Similarly, the right-hand side vector \mathbf{F} of size $8N_v \times 1$ is given by

$$\mathbf{F} = \int_{\Omega} \mathbf{\Phi}^T \mathbf{f}(\mathbf{u}^h) dx. \quad (4.7)$$

Regarding the time discretization, we denote the numerical approximation of the solution at $t = t_n$ by \mathbf{U}^n . Applying the backward Euler method to (4.4), we get

$$\mathbf{M} \frac{\mathbf{U}^{n+1} - \mathbf{U}^n}{\Delta t_n} + \mathbf{A} \mathbf{U}^{n+1} = \tilde{\mathbf{F}}, \quad (4.8)$$

where $\Delta t_n = t_{n+1} - t_n$ and $\tilde{\mathbf{F}}$ is an approximation of \mathbf{F} at time t_n . One simple choice for $\tilde{\mathbf{F}}$ is to explicitly compute \mathbf{F} using the value of \mathbf{u}^h at time t_n . We solve the resulting algebraic system using MATLAB.

4.2. Disease outcome. We mainly focus on the spatial distribution of three epidemiologically important quantities, namely dengue prevalence (%), new infection, and the total infection over an epidemic period, computed using our model as $100(u_6 + u_7)/u_{tot}$, $b\beta_m u_2 u_7 / u_{tot}$, and $\int_0^{t_f} \frac{b\beta_m u_2 u_7}{u_{tot}} dt$, respectively, where $u_{tot} = u_5 + u_6 + u_7 + u_8$. For our base case computation, we use $T_0 = 35^\circ\text{C}$, $T_1 = 10^\circ\text{C}$, $D_M = D_H = 0.0001$, and the remaining parameters as in Table 2.1. To allow the mobility to both cooler and warmer places, we introduce the initial infected population in the middle of the domain. Since, a dengue epidemic is usually over by 6 months, we take $t_f = 180$ days.

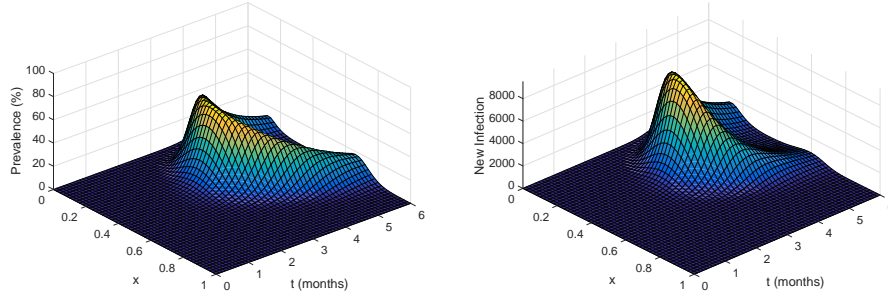


FIGURE 4.1. Spatio-temporal distribution of prevalence (left) and new infection (right) during an epidemic. Here, $T_m = 22.5^\circ\text{C}$ and $\Delta T = 25^\circ\text{C}$, and $D_M = D_H = 0.0001$.

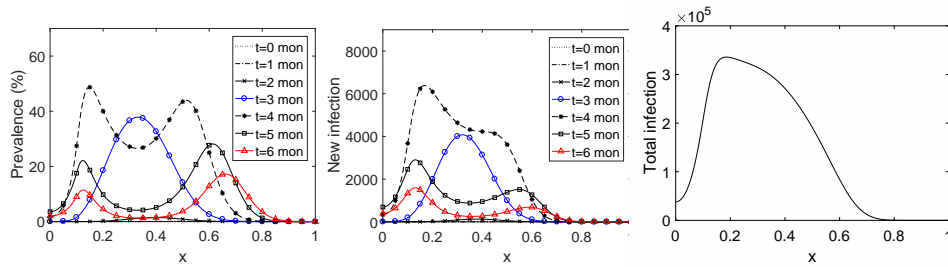


FIGURE 4.2. Distribution of prevalence (left) and new infection (middle) at different times and the total infection during an epidemic (right). Here, $T_m = 22.5^\circ\text{C}$ and $\Delta T = 25^\circ\text{C}$, and $D_M = D_H = 0.0001$.

After introduction of initial infected population in the middle of the domain, the prevalence and new infection increase in the middle for the first three months, and then they slowly appear to increase towards sides due to mobility of humans and vectors (Figs. 4.1, 4.2). Because of spatial heterogeneity of the temperature profile, the distribution eventually becomes asymmetric with more new infections generated towards warmer sides. As a result, the warmer place suffers from a higher total number of infections during the epidemic (Fig. 4.2, right). Compared to new infections and the total infection, the prevalence in 6 month remains more symmetric with slightly higher prevalence towards cooler place (Fig. 4.2, left). During the entire course of epidemic, the peak prevalence occurred at location $x = 0.27$ in

$t = 102$ days, and the peak new infection occurred at location $x = 0.26$ in $t = 105$ days.

4.3. Effect of temperature heterogeneity. To study how the spatial distribution of disease outcome is affected by temperature heterogeneity, we consider two different temperature profiles: one with the same mid value ($T_m = 0.5 * (T_0 + T_1)$) but different endpoint difference ($\Delta T = T_0 - T_1$) and another with the same ΔT but different T_m .

First, we fixed T_m at the base case ($T_m = 22.5^\circ\text{C}$), and changed ΔT from the base case ($\Delta T = 25^\circ\text{C}$) to a lower value, $\Delta T = 15^\circ\text{C}$ (Fig. 4.3, upper panel), and a higher value, $\Delta T = 35^\circ\text{C}$ (Fig. 4.3, lower panel). Initial increase of prevalence (Fig. 4.3, left) as well as new infection (Fig. 4.3, middle) in the middle region are higher for higher ΔT . In a long run, infection spreads widely towards the sides for lower ΔT , while for higher ΔT , the infection is more concentrated in the middle region with less spread towards the sides. This is because, with higher ΔT , the temperatures at two ends become either too low or too high, thereby causing less infection. As a result, the total infection during epidemic is more widely distributed across the region for a lower value of ΔT (Fig. 4.3, right). This shows that a uniform temperature across space has tendency to decrease infection in the middle for the initial period of infection, but has tendency to spread widely across space during the epidemic.

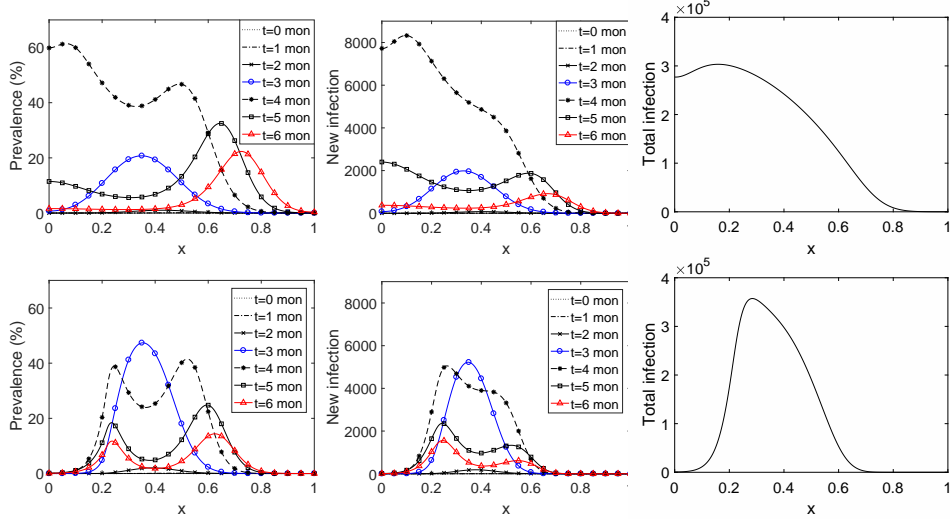


FIGURE 4.3. Distribution of prevalence (left) and new infection (middle) at different times and the total infection during an epidemic (right) for the end point temperature difference $\Delta T = 15^\circ\text{C}$ (upper panel) and $\Delta T = 35^\circ\text{C}$ (lower panel). Here $T_m = 22.5^\circ\text{C}$ and $D_M = D_H = 0.0001$.

Next, we fixed $\Delta T = 25^\circ\text{C}$ (base case), and considered two temperature profiles with a lower mean temperature ($T_m = 15^\circ\text{C}$) (Fig. 4.4, upper panel) and a higher mean temperature ($T_m = 30^\circ\text{C}$) (Fig. 4.4, lower panel). In this case, the infection

did not grow in the middle for lower T_m as opposed to the pattern seen in higher values of T_m . Both prevalence (Fig. 4.4, left) and new infection (Fig. 4.4, middle) diffuse towards warmer temperature side for lower T_m and cooler temperature side for higher T_m . Because of the difference in mean temperature, the total infection during epidemic is more concentrated towards the warmer side for lower T_m (Fig. 4.4, upper panel, right) and towards the cooler side for higher T_m (Fig. 4.4, lower panel, right). Therefore, for the same endpoint temperature difference ΔT , the lower the mean temperature, the higher the infection concentration towards the warmer place.

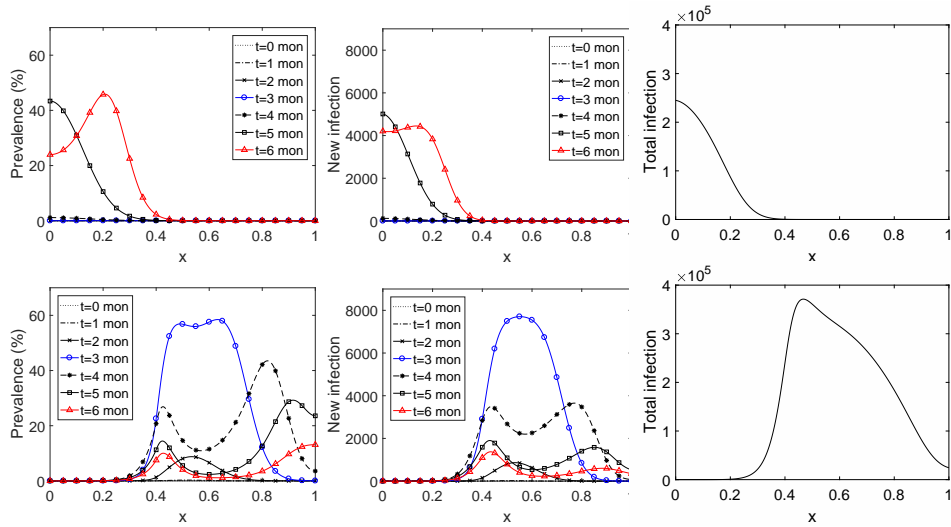


FIGURE 4.4. Distribution of prevalence (left) and new infection (middle) at different times and the total infection during an epidemic (right) for the mean temperature $T_m = 15^\circ\text{C}$ (upper panel) and $T_m = 30^\circ\text{C}$ (lower panel). Here $\Delta T = 25^\circ\text{C}$ and $D_M = D_H = 0.0001$.

4.4. Effect of human and vector mobility. Due to lack of information about spatial mobility of disease among mosquito population and human population, we used the same value of D_M and D_H for the base case. In this section, we study how the disease outcomes are changed if the ratio of these diffusion coefficients is altered (Fig. 4.5). Clearly there are some effects on disease outcomes when the ratio is changed to 10-fold lower mosquito mobility, i.e. $D_M/D_H = 0.1$ (Fig. 4.5, upper panel) and to 10-fold higher mosquito mobility, i.e. $D_M/D_H = 10$ (Fig. 4.5, lower panel). However, the effect seems less pronounced compared to the effects of temperature heterogeneity. Therefore, while mobility is significantly effective in spatial spread of dengue, it is less sensitive to whether the disease moves through vector movement or human movement.

5. Conclusion. Epidemiological data indicate that dengue fever is one of the most rapidly spreading vector-borne diseases, thus spatial expansion of dengue epidemic

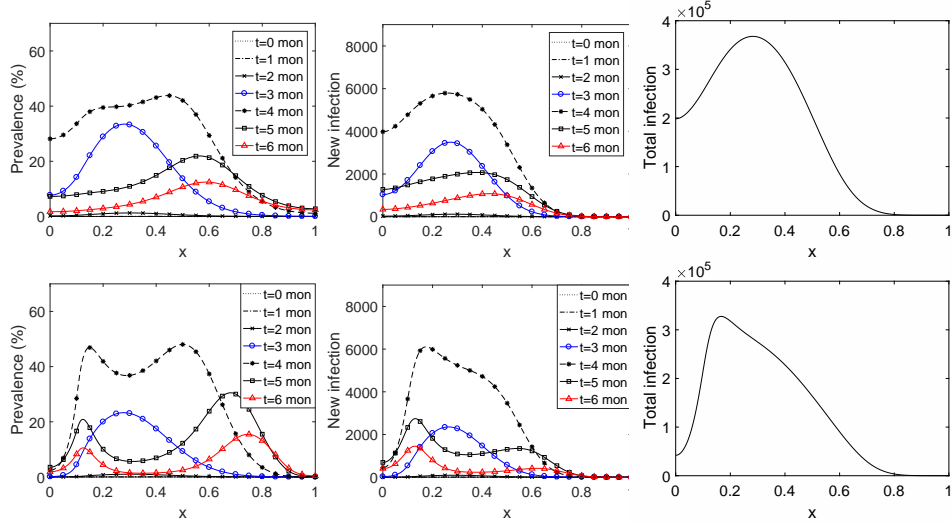


FIGURE 4.5. Distribution of prevalence (left) and new infection (middle) at different times and the total infection during an epidemic (right) for $D_M/D_H = 0.1$ (upper panel) and $D_M/D_H = 10$ (lower panel). Here $T_m = 22.5^\circ\text{C}$ and $\Delta T = 25^\circ\text{C}$.

poses serious public health concerns worldwide. In this paper, we provide a mathematical model to describe spatial spread of dengue. Our model particularly focuses on spatial heterogeneity of environmental temperature along with human and vector mobility. Experimentally derived temperature-dependent entomological and dengue dynamics parameters are some of the important features of our model.

We used our model to explicitly formulate the basic reproduction number ($\bar{\mathcal{R}}_0$) that provides temperature-dependent condition for the disease to die out ($\bar{\mathcal{R}}_0 < 1$) or infection to persist ($\bar{\mathcal{R}}_0 > 1$) in a spatially homogeneous environment. In a case of homogeneous environment, we identified an optimal range of temperature for which dengue epidemic occurs (i.e. $\bar{\mathcal{R}}_0 > 1$); dengue can not spread if the temperature is too cold or too hot. For a case of spatially heterogeneous environment, we provide theoretical formulations of two threshold indices, mosquito reproduction number (\mathcal{R}^M) and infection invasion threshold (\mathcal{R}_0). We discuss the case $\mathcal{R}^M < 1$ that presumably corresponds to the global stability of DFE E_0 (see Remark 3.1), in which mosquito population gets eradicated along with dengue. This situation is related to prevention programs that target to destroy mosquito population. Furthermore, we prove that $\mathcal{R}^M > 1$ and $\mathcal{R}_0 < 1$ provide the global stability of DFE E_1 , in which dengue is eradicated in the presence of mosquito population. In this case, we also prove that the disease persists for $\mathcal{R}_0 > 1$. The infection invasion threshold \mathcal{R}_0 includes dengue related prevention strategies along with mosquito controls.

We also performed thorough simulation of the model to study effects of the temperature heterogeneity and human-vector mobility on disease outcomes, including prevalence, new infections and the epidemic size (the total infection during an epidemic). We find that both temperature heterogeneity and human-vector mobility play important role in spatial spread of dengue. While the mobility (human or

vector) significantly affects the spread of disease, whether the vector moves faster or the human moves faster does not seem to play major role in the dengue spread. Most importantly, our results show that the environmental temperature heterogeneity has extremely important role in altering disease outcomes. In particular, temperature profiles with lower mean cause the spread of dengue towards warmer places and less heterogenous temperature profiles cause the spread of dengue widely across space during the epidemic.

While the threshold indices developed and simulation results generated in our study can be useful to design prevention and control strategies to reduce dengue spread, we acknowledge some limitations of our study. Because the main focus of this study is to investigate the effects of spatial heterogeneity of temperature, we ignored possible change of the temperature over time. Thus, our results are more relevant to places where the temperature remains approximately constant throughout the epidemic season. To incorporate a temporal change of the temperature, our model needs to be improved by considering spatial-temporal dependent parameters, which we plan to pursue in our future work. Our parameters are obtained from the limited data sets and limited studies. Therefore, there might be some uncertainties on parameter estimates, particularly those related to human and vector mobility. Finally, prevention and control strategies need to be incorporated explicitly in the model to accurately evaluate those strategies.

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